Mitral Valve Prolapse: Clinical Features, Laboratory Abnormalities, Complications, and Prognosis

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Mitral valve prolapse is being diagnosed with increasing frequency now that its characteristic clinical features, including auscultatory abnormalities, and echocardiographic manifestations have been identified. This article describes the valvular pathology, physical findings, and electrocardiographic, echocardiographic, and angiographic features which may be observed in patients with mitral valve prolapse. Potential complications attributable to mitral valve prolapse are discussed and its prognosis is addressed. While mitral valve prolapse may be complicated by serious ventricular arrhythmias, sudden death, endocarditis, or sudden or progressive mitral regurgitation requiring valve replacement, it is frequently asymptomatic and is usually associated with a relatively benign prognosis.

Mitral valve prolapse has been identified as a clinical syndrome for less than 20 years. The long delay in its recognition is rather remarkable given the great prevalence of the physical findings associated with it.

Historical Aspects

The auscultatory abnormalities of mitral valve prolapse, including midsystolic clicks and late systolic murmurs, have been recognized since the late 1800s.[1,2] However, although several authors postulated a mitral valve etiology for those sounds,[2,3] most authors considered them to be of extracardiac origin. In 1961, Reid,[4] noting the frequent association of a murmur with midsystolic clicks, raised again the possibility of an intracardiac or intravascular origin. He proposed pathophysiologic mechanisms for both the clicks and the late systolic murmurs[4]:

> It does not seem illogical to assume that the valves can be competent at an early stage of systole and become incompetent later, since the design of the artrioventricular valve is unique: the apposition of the cusps is maintained via chordae by muscles which themselves are attached to the moving part of the pump, ie, the ventricular muscle. The papillary muscles contract in systole and so apposition of the cusps is maintained. It is conceivable that a disturbance of this action, for example, by insufficient contraction of a papillary muscle, or by elongation of a chorda, may result in a slackening of

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the chorda in mid-systole. At this stage the high-pressure gradient across the valves might be expected to snap a slack chorda taut, producing a sound. The attached cusp might then still be competent, producing no murmur; or incompetent, with the production of a murmur that should extend to the second sound or into diastole, as far as mitral or tricuspid re-opening.

Reid's hypothesis of mitral valve origin was confirmed in 1963 by Barlow and his associates.[5] They demonstrated the association of clicks, late systolic murmurs, and electrocardiographic abnormalities with angiographic mitral valve prolapse. Intracardiac phonocardiograms subsequently documented that the clicks and late systolic murmurs arose from the inflow region of the mitral valve.[6,7] Further documentation of mitral etiology has resulted from observations correlating the behavior of the clicks and murmurs with changes in left ventricular volume and contractility, from angiographic demonstration of mitral regurgitation in patients with late systolic murmurs, and from echocardiographic studies demonstrating abnormalities of mitral valve movement in patients with typical auscultatory findings.[8-19]

Multiple names have been applied to the syndrome of mitral valve prolapse. These include the auscultatory-electrocardiographic syndrome, ballooning of the mitral valve leaflets, billowing posterior leaflet syndrome, Barlow's syndrome, click syndrome, click murmur syndrome, "floppy" valve syndrome, idiopathic mitral valve prolapse, mitral valve prolapse, mitral valve prolapse syndrome, mitral valve prolapse-click syndrome, myxomatous degeneration of the mitral valve, over-shooting mitral leaflets, prolapsing mitral leaflet syndrome, and systolic click-late systolic murmur syndrome.[10] In addition, it is likely that many patients previously described as having DaCosta's syndrome or neurocirculatory asthenia may have been patients with mitral prolapse.

Pathology

The pathology of the mitral valve prolapse syndrome has not been extensively studied, since few patients in whom the syndrome has been recognized prior to death have come to autopsy. The valvular pathology, seen in autopsy and operative specimens, is almost certainly skewed toward more severe myxomatous degeneration.

The normal cardiac valves consist of fibrosa and spongiosa components.[11] The spongiosa normally contains acid mucopolysaccharides.[10,11] In mitral valve prolapse, there is an increase in the amount of spongiosa and, therefore, in the amount of acid mucopolysaccharide in the valve.[11,20] The normally dense collagenous fibrosa becomes replaced by this loose, metachromatically staining myxomatous tissue.[10,21-23] The fibrous disintegration may advance toward and involve the annulus as well as the chordae.[23] No inflammation is generally apparent.[10] Grossly, the valve appears voluminous in area, capable of prolapsing into the left atrium.[21,22] The leaflets are usually at least slightly thickened[23] and the chordae, although occasionally thickened, are generally thinned and prone to rupture.[22,23] Both mitral valve leaflets are often involved but selective involvement of the posterior leaflet may be observed.[22] The lack of commissural fusion and fibrous contractions of the chordae, the increase in cusp area, and the lack of appreciable increase in fibrous tissue differentiate mitral valve prolapse from other valvular abnormalities, including rheumatic deformity.[11,21] Fibrin deposition without inflammatory reaction may be seen on one or both mitral cusps, often in association with leaflet tears.[22] Thrombi may be seen on the posterior wall of the left atrium, adjacent to the insertion of the posterior mitral valve leaflet.[22] Such fibrin deposits and thrombi may have an important etiologic role in the neurologic symptoms which may be observed in patients with prolapse. There may be fibrous adhesions of chordae to the left ventricular endocardium, and papillary muscle fibrosis may be seen.[22] The mitral valve annulus is often dilated, sufficient to cause mitral regurgitation.[24] Such gross annular dilatation is generally seen only in patients with mitral valve prolapse and/or Marfan's syndrome.[24] Pathologic involvement of the tricuspid valve is seen in approximately one fourth of patients.[22]

Prevalence

Mitral valve prolapse, diagnosed by characteristic pathologic findings, physical features, or echo-

cardiographic patterns, appears to be a common abnormality. Autopsy studies have documented a one to five percent prevalence of "floppy valve" or "ballooning deformity" of the mitral valve.[22,23] Auscultatory, phonocardiographic, and/or echocardiographic studies have documented prevalences ranging from 0.33 to 21 percent.[10,25-29] There is a female preponderance in most series,[10,11,30] but signs of prolapse are commonly seen in men as well.[11,25,29] This syndrome may be seen in patients of different races and of all ages,[10,11] including the newborn.[26]

Etiology

The etiology of mitral valve prolapse is not known. Family studies demonstrate an autosomal dominant mode of transmission, with decreased penetrance in males.[8,31] There may be delayed appearance of auscultatory abnormalities.[11] The syndrome may also occur sporadically. The association of mitral valve prolapse with abnormalities of the thoracic skeleton[29,32,33] and with certain dermatoglyphic patterns[34] suggests the influence of some genetic or environmental factor in the fifth to sixth gestational week.[33]

Clinical Presentation

Many patients with mitral valve prolapse are asymptomatic. They may be detected by the presence of auscultatory or electrocardiographic abnormalities or because of a family history of mitral valve prolapse or its complications, such as sudden death.[11]

Chest pains, dyspnea, fatigue, dizziness, syncope, palpitations, transient ischemic attacks, and psychological disturbances, however, are frequently found in patients with mitral valve prolapse. In reported series of patients with mitral valve prolapse, some 75 to 87 percent of patients have one or more of those symptoms related to mitral valve prolapse.[9,10,30,35,36] The available studies, however, probably greatly overestimate the true prevalence of symptoms since they are based on patients who are often identified because of symptoms, electrocardiographic abnormalities, or complications of mitral valve prolapse. Large population surveys, including symptomatic and asymptomatic individuals, would have to be performed in order to determine the true prevalence of symptoms.

Chest pain has been described in 35 to 72 percent of patients with documented mitral valve prolapse.[9,30,35] Occurring in patients both with and without electrocardiographic changes,[37] the chest pain is often ill defined. It may be sharp and jabbing, located in the left precordium, and lasting seconds to minutes, or may be a dull precordial ache which persists for hours to weeks.[9,10] It usually occurs without relationship to exertion.[35] Its quality and lack of precipitation by exertion generally permit differentiation from ischemic pain. The discomfort, however, may have qualities typical of angina or of pericardial pain,[10] produced either by mitral valve prolapse or by co-existing coronary artery or pericardial disease.

The etiology of chest discomfort in mitral valve prolapse is not clear. The electrocardiographic abnormalities[9,11,12,23,37] and abnormalities of lactate extraction[10] which may be observed in patients with mitral valve prolapse raise the possibility of an ischemic etiology. Excessive traction of the chordae on the papillary muscles could perhaps result in focal ischemia. Propranolol may effectively treat the pain in some patients. Propranolol likely decreases the magnitude of mitral valve prolapse by decreasing left ventricular contractility and heart rate and by increasing left ventricular volume. Many patients with mitral valve prolapse, however, complain of excessive fatigue and depression on even small doses of propranolol.[10] Symptomatic improvement has been observed following mitral valve replacement in occasional individuals.[10]

Dyspnea is a common complaint, noted by 30 to 38 percent of patients.[30,35] It is not usually associated with signs of congestive heart failure.[11] Although many individuals with mitral valve prolapse have deformities of the thoracic skeleton, including pectus excavatum, straight back, and scoliosis[29,32,33,38] and 50 to 63 percent have been shown to have decreases in steady-state diffusing capacity or increases in residual volume on pulmonary function testing,[38] no relationship between dyspnea and chest wall deformities or abnormali-

ties of pulmonary function have been noted.[38] Fatigue is also a common complaint, noted by 42 percent of patients.[35]

Palpitations are noted by 44 to 49 percent of patients,[9,30,35,36] and lightheaded spells, dizziness, and syncope by approximately 30 percent.[9,35,36] While such symptoms are commonly produced by a variety of atrial and ventricular arrhythmias or by sinus bradycardia, in some patients no correlation is noted between the above symptoms and the underlying rhythm.[39]

Psychological disturbances occur frequently in patients with mitral valve prolapse. Manifestations of psychosis, hyperventilation, psychoneurosis, personality disorders, hysteria, hypochondriasis, depression, psychopathic deviation, schizophrenia, and psychasthenia may be noted in 15 to 38 percent of the patients.[10,30,35]

Recent reports have noted the association between mitral valve prolapse and recurrent transient ischemic attacks or partial strokes, particularly in young individuals.[9,40-47] The familial occurrence of cerebral ischemic events in association with mitral valve prolapse has been documented.[40,44] In one study,[40] mitral valve prolapse was demonstrated in 40 percent of 60 patients less than 45 years of age who had transient ischemic attacks or partial strokes. The prevalence of mitral valve prolapse in an age matched control group was significantly lower at 6.8 percent. The 5.7 percent prevalence of echocardiographic mitral valve prolapse in 141 patients with similar neurologic abnormalities over the age of 45 years did not differ from that of 7.1 percent in an age matched control group, however, suggesting age dependence.[40] It is postulated that embolization of fibrin deposits, which may be seen at autopsy on the left atrial wall or on the mitral valve in patients with mitral valve prolapse, may be responsible for neurologic events.[10,22] Two dimensional echocardiography has demonstrated masses of echoes on the mitral valve leaflets or within the angle formed by the left atrial wall and the posterior mitral valve leaflets in some patients with mitral valve prolapse suffering transient ischemic attacks or strokes.[44,45] Those echoes could conceivably represent thrombi responsible for embolic symptoms. In some patients, atrial arrhythmias or endocarditis may be alternative explanations for central nervous system emboli.[41,42] The role of anticoagulant and antiplatelet therapy remains to be clarified.

Symptoms have been reported in a high percentage of patients with the auscultatory-silent form of mitral valve prolapse.[10] This, however, is not unexpected since most patients without clicks or murmurs will have come to medical attention because of symptoms or complications of mitral valve prolapse.

Physical Examination

The general physical examination is frequently normal. However, many patients with mitral valve prolapse demonstrate an asthenic body build, a high arched palate, joint laxity, or abnormalities of the thoracic skeleton.[10,29,32,33] In two series of 24 and 64 patients manifesting auscultatory findings of mitral valve prolapse, 61 to 75 percent of patients had a pectus excavatum, straight back, and/or severe scoliosis.[32,33] Unusual dermatoglyphic patterns may be seen in approximately one fifth of patients with mitral valve prolapse. The presence of four or more digital arches or the presence of arches on the fourth or fifth digits appears unique to patients with mitral valve prolapse.[34] Mitral valve prolapse may be associated with specific diseases of connective tissue, including Marfan's syndrome, Ehlers-Danlos syndrome, osteogenesis imperfecta, pseudoxanthoma elasticum, and relapsing polychondritis. In those patients, typical clinical features of the connective tissue disease will also be observed.[10,12]

On cardiac examination, the location and quality of the apical impulse are generally normal. Occasionally, systolic retraction of the apex impulse may be palpated and can be recognized on an apex cardiogram.[10] Characteristic auscultatory features are generally present, including mid- or late systolic click(s), late systolic murmurs, with or without associated click(s), and holosystolic murmurs. These findings generally first suggest the diagnosis of prolapse. In Jeresaty's series of 350 patients with mitral valve prolapse,[10] isolated mid-late systolic clicks were found in 53.1 percent, early clicks in 1.1 percent, midsystolic clicks and late systolic murmurs in 17.2 percent, late systolic murmurs alone in 2 percent, precordial honks in 1 percent,

Table 1. Effects of Positional Changes and Maneuvers on the Auscultatory Findings of Mitral Valve Prolapse

	Click(s)	Murmur
Inspiration	Move Toward S_1	Begins earlier in systole Intensity may be decreased
Expiration	Move Toward S_2	Begins later in systole
Sitting	Move Toward S_1	Begins earlier in systole Intensity may be decreased
Standing	Move Toward S_1	Begins earlier in systole Intensity may be decreased
Valsalva strain phase	Move Toward S_1	Begins earlier in systole Intensity may be decreased
Valsalva release phase	Move Toward S_2	Begins later in systole
Tilting	Move Toward S_1	Begins earlier in systole Intensity usually decreased
Inhalation of amyl nitrite	Move Toward S_1	Begins earlier in systole Intensity usually decreased
Hand Grip	Move Toward S_2	Begins later in systole Intensity usually increased
Squatting	Move Toward S_2	Begins later in systole Intensity usually increased
Passive leg raising	Move Toward S_2	Begins later in systole Intensity may be increased

and pansystolic murmurs in 8.6 percent. "Silent" mitral valve prolapse, demonstrated by means other than auscultation and phonocardiography, was present in 16.9 percent. The auscultatory findings of mitral valve prolapse are frequently quite variable. Findings may be transient, with murmurs and/or clicks appearing and disappearing in any given patient. Often clicks and murmurs may not be heard at rest but may be brought out by postural and/or pharmacologic maneuvers. Mitral clicks are best heard at the apex or just medial to it. Being high pitched, they are generally heard best with the diaphragm and are most easily appreciated if the examiner listens selectively for high pitched sounds. Early systolic clicks are infrequent but may occur in patients with early onset of systolic prolapse, often in association with a holosystolic murmur. Although an isolated mid-late systolic click may occasionally develop during the course of acute myocardial infarction,[48] a mid- or late systolic click is thought to be highly specific for the diagnosis of idiopathic mitral valve prolapse.[10] The differential diagnosis of an early or mid-late systolic click includes an ejection sound of semi-lunar valve or great vessel origin, a diastolic gallop, opening snap, widely split second sound, and systolic clicks related to pneumothorax, pericarditis, myxoma, malfunctioning heterograft valves, idiopathic hypertrophic subaortic stenosis, left ventricular aneurysm, and aneurysms of the membranous septum in association with a ventricular septal defect.[10,11] Characteristic mobility of the click with postural and/or pharmacologic maneuvers is the key to diagnosis[12] (Table 1). Inhalation of amyl nitrite and performance of maneuvers such as sitting, standing, and the Valsalva maneuver, which are associated with a decrease in left ventricular systolic volume, cause an earlier appearance of the click in systole.[10,29,30] Increases in afterload or venous return, produced by hand grip, squatting, or passive leg raising, generally cause the click to move

toward the aortic second sound.[10] The intensity of the click is dependent upon left ventricular systolic pressure and left ventricular contractility.[11]

The murmur of mitral valve prolapse may be holosystolic or confined to mid- and late systole. Pansystolic murmurs generally imply greater degrees of mitral regurgitation.[10] The murmurs typically extend to or through the aortic second sound and may have a uniform, crescendo-decrescendo, or crescendo pattern.[11,12] A decrescendo murmur which ends prior to the aortic second sound may be present in patients with severe mitral regurgitation.[11] A whooping or honking quality may be apparent.[10] Unlike the mid-late systolic click, pansystolic and late systolic murmurs are not specific for mitral valve prolapse, being present as well in other conditions such as rheumatic mitral regurgitation, mitral annular calcification, papillary muscle dysfunction and idiopathic hypertrophic subaortic stenosis (IHSS).[10,48] However, as with prolapse clicks, characteristic changes in the intensity and timing of a mitral prolapse murmur with postural and/or pharmacologic maneuvers may enable its differentiation from murmurs of other etiologies[10-12] (Table 1). The intensity of a murmur generally depends on the level of aortic and, therefore, of left ventricular systolic pressure.[10] The timing of prolapse and, therefore, of the onset of the murmur depends upon left ventricular contractility and upon left ventricular volume at the onset of systole. Factors which result in a decrease in left ventricular volume, such as inspiration, sitting, standing, performance of the Valsalva maneuver, and inhalation of amyl nitrite, cause an earlier appearance of the murmur.[10,11] The murmur, however, while earlier, may be of lesser intensity due to the associated decrease in left ventricular systolic pressure.[10,11] Squatting, which increases afterload and venous return and decreases heart rate, may increase the intensity of the murmur but causes it to move toward the second sound. Inhalation of amyl nitrite results in a decrease in afterload and an increase in heart rate and contractility. The murmur of mitral valve prolapse will consequently begin earlier but the associated decrease in systemic arterial pressure will generally cause the intensity of the murmur to diminish.

Changes in the murmur of mitral valve prolapse are often similar to those produced by similar maneuvers in patients with IHSS.[11,12] However, the Valsalva maneuver generally produces no increase in intensity of the prolapse murmur as compared to a marked increase in the loudness of the usual IHSS murmur.[11] In addition, the murmur of IHSS increases in intensity in a post-extrasystolic beat while, in mitral valve prolapse, generally no increase is observed.[11] Holosystolic murmurs in patients with mitral valve prolapse may be due to mitral annular dilatation or to chordal rupture, in addition to overshooting of the mitral leaflets.

The Electrocardiogram

The electrocardiogram is generally normal in patients with mitral valve prolapse.[11,37] However, ST-T wave abnormalities, prolongation of the QT interval, and arrhythmias may be seen. Q waves compatible with myocardial infarction have been observed only rarely in the presence of normal coronary arteries.[10] The most common electrocardiographic abnormality is full or partial T wave inversion, usually present in the inferior leads but occurring occasionally in the right, mid, or left precordial leads.[9,11,12,30,37] Standing, inhalation of amyl nitrite, exercise, phenylephrine infusion, and pacing may accentuate the T wave changes or cause the appearance of new T wave changes in a patient with normal resting T waves.[9,11,12,30] ST segment flattening and prominent U waves may be present.[9,37] The prevalence of QT prolongation has varied dramatically, from less than 1 percent to 60 percent in the various series in which QT intervals have been reported.[9,30,36,37] The etiology of the electrocardiographic changes is not known. While it has been postulated that they may be due to left ventricular or papillary muscle ischemia, it is curious that the presence of chest pain and arrhythmias may not correlate with electrocardiographic abnormalities.[11]

There is a high prevalence of electrocardiographic abnormalities in patients with auscultatory-silent mitral valve prolapse.[10] This high prevalence is to be expected, however, because the diagnosis in many patients was made following the recognition of electrocardiographic abnormalities, including arrhythmias.

Exercise tolerance testing not uncommonly produces electrocardiographic changes compati-

ble with ischemia in patients with idiopathic mitral valve prolapse and normal coronary arteries.[10,37] Stress myocardial scintigraphy with thallium 201 has shown variable results, but scans have been normal in most patients in the absence of coronary artery disease.[10] Ventricular arrhythmias may be precipitated by exertion.[9,37,49] Many patients fail to achieve their target heart rate during exercise,[9] due to the onset of chest pain, dyspnea, or fatigue.

Arrhythmias have been observed in 45 to 75 percent of prolapse patients[30,36,39] and include ventricular premature contractions,[12,30,39] atrial premature contractions,[12,30,39] ventricular tachycardia,[27,30,39,50] supraventricular tachycardias including atrial fibrillation, atrial flutter, and atrial tachycardia,[12,27,29,30,39,50] marked sinus arrhythmia,[12] and sinus bradycardia and the bradycardia-tachycardia syndrome.[12,51] In a large review of 589 patients, premature ventricular contractions, both unifocal and multifocal, were seen in 55 percent, premature atrial contractions in 45 percent, supraventricular tachycardia in 6.1 percent, ventricular tachycardia in 6.3 percent, and sudden death in 1.4 percent of patients.[36] Arrhythmias may be precipitated by exertion[37,49] but are usually seen at rest or during ordinary activities, including sleep.[39,49] While arrhythmias are often responsible for the symptoms of palpitations, dizziness, and syncope, the latter symptoms may also occur in the absence of a change in underlying rhythm.[11,39] The occurrence of ventricular tachycardia and ventricular fibrillation has been greater in those patients with electrocardiographic abnormalities of repolarization or with ventricular ectopic beats on routine electrocardiogram.[39,49,50] The diagnosis of mitral valve prolapse has been made prior to episodes of life threatening arrhythmias in a minority of patients.[49]

While it is not known whether the presence of ventricular ectopic activity, short of ventricular tachycardia and ventricular fibrillation, increases the risk of sudden death or whether long-term anti-arrhythmic therapy is effective in decreasing the risk of sudden death, anti-arrhythmic therapy should be considered for patients with advanced and/or symptomatic ventricular ectopy. Propranolol, which may diminish the magnitude and duration of systolic mitral valve prolapse and can result in shortening of the QT interval, may be effective in suppressing ventricular ectopic activity, either alone or in association with other anti-arrhythmics, such as quinidine and diphenylhydantoin.[10,36,37,49] Mexiletine, aprindine, and disopyramide have proven effective in individual patients.[10] A systematic approach to the work-up and management of ventricular arrhythmias, including the monitoring of response to treatment, is crucial.

Echocardiography

Echocardiography is currently the procedure of choice for the diagnosis of mitral valve prolapse. It is noninvasive and appears to have a specificity for idiopathic mitral valve prolapse superior to that of angiographic techniques. The lack of a precise standard, short of pathologic evaluation, with which to judge diagnostic techniques, however, makes estimation of true sensitivity and specificity impossible.

The normal mitral valve demonstrates a gradual anterior movement in systole, due to the forward movement of the entire mitral valve ring.[18] If the echocardiographic transducer is placed perpendicularly on the chest or is angled slightly cephalad to record the mitral valve leaflets, a gradual anterior systolic movement of the anterior and the posterior leaflets toward the transducer will be recorded in normal individuals. Two abnormalities of mitral valve systolic movement, observed by M-mode and cross-sectional echocardiography, have been found to correlate with the auscultatory, angiographic, and pathologic findings of mitral valve prolapse.[9,13,16,19,27,28] They are pansystolic posterior sagging of the mitral leaflets and abrupt, posterior movement of one or both leaflets beginning in mid to late systole[8,13-19,28] (Figure 1). Both patterns may occasionally be observed in different areas of a scan in any given patient, and the timing and duration of echocardiographic prolapse may change with alterations in left ventricular volume.[14] The pattern of late systolic prolapse appears to be more common than that of pansystolic mitral prolapse.[9,27] The onset of the click or murmur usually occurs simultaneously with the abrupt posterior movement of the mitral valve leaflets.[11,15] Multiple systolic echoes are generally recorded, due to leaflet redundancy.[11]

Unfortunately, the abnormal echocardiographic

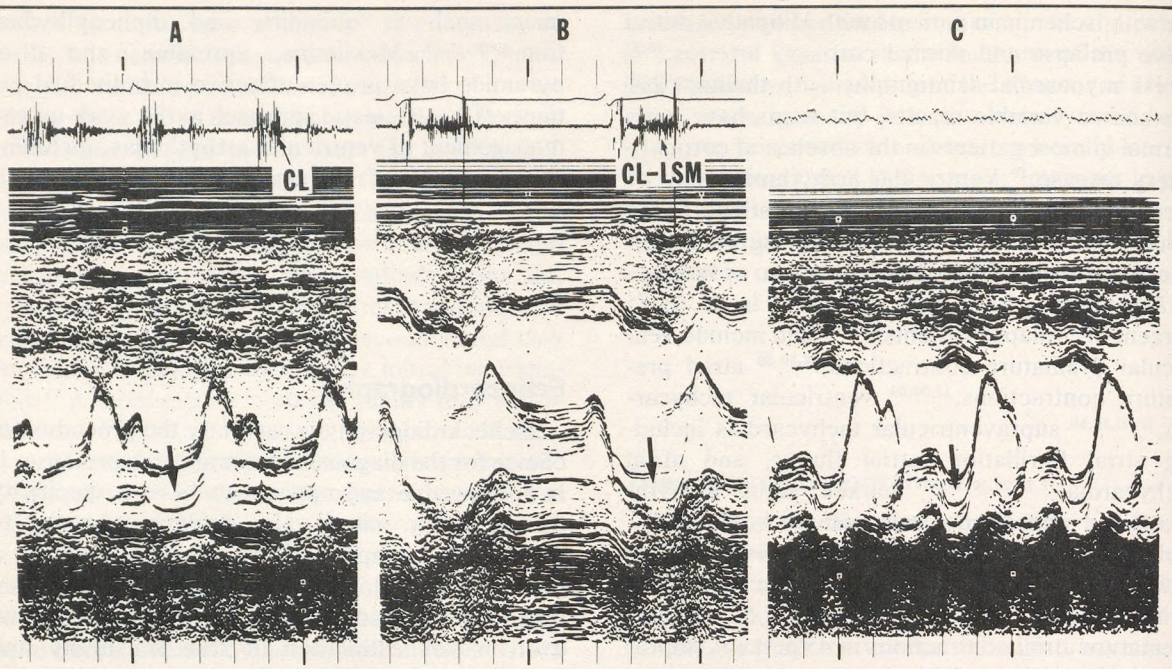

Figure 1. Echocardiographic findings in patients with mitral valve prolapse. Pansystolic prolapse is seen to be associated with an early non-ejection click (CL) in panel 1-A and with a click-late systolic murmur (CL-LSM) in 1-B. It may also be associated with a holosystolic murmur or no auscultatory findings may be apparent (not illustrated). The mid-late systolic posterior movement of the mitral valve leaflets (1-C) was associated with a mid-late systolic click (not illustrated). The large black arrows point to the prolapsing mitral valve leaflets

patterns of mitral valve prolapse are neither perfectly sensitive nor perfectly specific for the diagnosis of idiopathic mitral valve prolapse. The echocardiogram may appear normal in up to 20 percent of patients with classic auscultatory findings of prolapse[10,11,27,29,50] and is more likely to be normal in patients with isolated clicks than in those with clicks and murmurs.[11,28] The failure to appreciate mitral valve prolapse by echocardiographic techniques may be explained by the failure of the ultrasound beam to pass through prolapsing sections of the mitral valve leaflets or by the failure to direct the beam perpendicularly to the prolapsing leaflets. False positive studies may also occur, usually with the pattern of pansystolic sagging. A high transducer position on the chest frequently results in the appearance of pansystolic posterior movement of the mitral valve leaflets. This is because the entire mitral valve ring will move inferiorly relative to the transducer in systole.[8,20] A diagnosis of pansystolic mitral valve prolapse can be made, therefore, only if the ultrasound beam is directed perpendicularly to the mitral valve leaflets or is angled superiorly to record the mitral valve. Even with correct transducer placement, false positives may still occur. For example, patients with pericardial effusion may have sagging of the mitral valve leaflets independent of mitral valve prolapse.

Chordal rupture is frequently associated with mitral valve prolapse and may be recognized echocardiographically.[19,52] In some cases, the pattern of chordal rupture may mimic that of mitral valve prolapse alone. Excluding patients with evidence of Marfan's syndrome, 1.8 percent of patients with mitral valve prolapse have been found to have

aortic root enlargement and 3 percent to have tricuspid valve prolapse.[52]

Catheterization Findings

Catheterization is rarely necessary to confirm the diagnosis of mitral prolapse in a typical patient.[12] Characteristic angiographic abnormalities may suggest the diagnosis, however, and catheterization may be indicated to exclude coincident coronary arterial, myocardial, or pericardial disease.

Angiographically, mitral valve prolapse is characterized by systolic protrusion of one or both mitral valve leaflets above the plane of the mitral annulus.[12] The posterior leaflet is almost always involved, with or without the anterior leaflet.[10] Isolated prolapse of the posteromedial scallop of the posterior leaflet is frequently observed.[9] Mitral regurgitation may be seen when coaptation of the mitral leaflets is incomplete.

Unfortunately, the angiographic pattern of mitral prolapse is not specific for idiopathic mitral prolapse. Normal individuals may show systolic "lipping" in the right anterior oblique view,[10] and patients with a variety of apparently unassociated cardiovascular abnormalities may demonstrate an angiographic pattern compatible with mitral prolapse. In a review of left ventriculograms in 336 consecutive patients,[53] angiographic mitral valve prolapse was seen in 43 percent of all patients, including 100 percent of six patients with the auscultatory click-murmur syndrome, 40 percent of patients with ischemic heart disease, 32 percent with rheumatic heart disease, 16 percent with cardiomyopathy, 42 percent with congenital heart disease, and 60 percent with chest pain and normal or nearly normal coronary arteries. Clicks and murmurs were observed in 5 of 22 patients with the pattern of moderate to severe angiographic mitral prolapse.[53] Abnormalities of the left ventricular contraction pattern have been observed in 28 to 82 percent of patients with the angiographic pattern of mitral prolapse.[54,55] Those include a ballerina foot pattern, produced by vigorous posteromedial contraction with anterior convexity, an hourglass pattern produced by vigorous ring-like contraction of the mid-left ventricle, decreased long axis shortening, posterior akinesia, and cavity obliteration.[55] Some investigators have suggested that contraction abnormalities may be the primary problem in mitral prolapse, producing secondary myxomatous changes in the mitral valve leaflets. However, as not all patients with mitral prolapse have angiographically demonstrable abnormalities of left ventricular contraction and as the pattern of left ventricular contraction may revert to normal following mitral valve replacement, it is more likely that the mitral valve abnormalities are primary and result in excessive traction on the papillary muscles, leading to abnormal contraction patterns.[11] Despite the prevalence of abnormal left ventriculograms, overall hemodynamic performance is usually normal, in the absence of significant mitral regurgitation.[10,12,54] Abnormalities of lactate metabolism have been reported,[10] raising the question of focal ischemia,[10] possibly related to traction on the papillary muscle.

Tricuspid valve prolapse has been observed during right ventriculography in 38 to 54 percent of patients tested.[9,55] The angiographic diagnosis of tricuspid valve prolapse, however, may be difficult given the normal variability of the tricuspid valve ring and tricuspid valve leaflets.[10]

Associated Abnormalities

Multiple diseases have been reported in association with mitral valve prolapse. Given the high prevalence of mitral valve prolapse in the general population, however, chance association with many of the diseases is likely. The reported association of idiopathic mitral valve prolapse with coronary artery disease and rheumatic heart disease is probably casual rather than causal.[10] Over 200 patients with secundum atrial septal defects in association with mitral valve prolapse have been reported.[10] While it is possible that this represents a chance association between two rather common abnormalities[11] or that the presence of a left to right atrial shunt may cause the appearance of prolapse, a true relationship probably exists.[10] In addition to connective tissue diseases such as Marfan's syndrome, Ehler's Danlos syndrome, osteogenesis imperfecta, pseudoxanthoma elasticum, and relapsing polychondritis, mitral valve prolapse has been reported in association with IHSS, Ebstein's anomaly of the tricuspid valve, Turner's syndrome, Wolff-Parkinson-White syndrome, and corrected transposition of the great vessels.[10,12]

Complications

At its extreme, mitral valve prolapse can predispose to malignant ventricular ectopy, causing recurrent dizziness or syncope, cardiac arrest, and sudden death; to endocarditis; and to either sudden, severe congestive heart failure related to chordal rupture or to progressive congestive heart failure secondary to chronic mitral regurgitation. The arrhythmias associated with prolapse have been described. Sudden death has been reported in over 25 patients with mitral prolapse and sustained ventricular fibrillation, successfully resuscitated, in another 21.[10] Episodes of sudden death or ventricular fibrillation may occur during exertion or at rest. There is frequently a history of prior syncope and of prior electrocardiographic abnormalities, including ST-T wave changes and ventricular ectopic activity.[10,56,57] Most patients in whom physical examinations were described were known to have murmurs, but sudden death has also been reported in a patient with an isolated click.[10] A familial tendency to sudden death in mitral valve prolapse has been noted.[11] Repair or replacement of the mitral valve has been performed in patients with ventricular arrhythmias refractory to medical management. While some patients have improved, surgery may not prevent recurrent ventricular fibrillation or sudden death or eliminate the need for continued anti-arrhythmic therapy.[12,58]

Multiple reports have documented the occurrence of bacterial endocarditis in patients with mitral valve prolapse.[7,10,11,56,59,60] The diagnosis of prolapse is often first made during admission for endocarditis.[60] Patients with murmurs are most commonly affected, but bacterial endocarditis has been reported in patients with clicks alone.[11,60] Chordal rupture may complicate infective endocarditis, resulting in increased mitral regurgitation.[22]

Congestive heart failure may complicate mitral regurgitation in patients with mitral valve prolapse. Indeed, mitral valve prolapse accounts for approximately 50 percent of patients currently requiring mitral valve replacement for congestive heart failure associated with pure mitral regurgitation.[20] Patients with murmurs are often asymptomatic for many years. However, once symptoms of congestive heart failure ensue, rapid deterioration is likely.[51] Sudden onset or severe worsening of symptoms of left heart failure is not uncommon[51] and is likely related to the extraordinarily high prevalence of chordal rupture noted at surgery.[10,20,22,23,51] Chronic progressive congestive heart failure may complicate chronic valvular insufficiency and mitral annular dilatation.

A high operative and five-year mortality has been noted, with congestive heart failure the major cause of death.[20] Operations should optimally be performed prior to the onset of left ventricular dysfunction. Partial valve dehiscence may require re-operation.[20]

Prognosis

An abnormality as prevalent as mitral valve prolapse must generally be quite benign since bacterial endocarditis, sudden death, and severe mitral regurgitation in young individuals are relatively rare. The available studies in the literature likely overestimate the frequency of symptoms and complications of mitral valve prolapse since they are based largely on patients seeking or coming to medical attention because of symptoms, abnormal physical findings, electrocardiographic changes, arrhythmias, and other complications of prolapse. Nevertheless, even in the series reported, the prognosis is generally benign with most patients showing no complications and no consistent progression of symptoms.[10,56,57,59,61]

In Jeresaty's summary of 373 patients reported in the literature and followed for a mean of 4.2 years, bacterial endocarditis occurred in 11 patients, sudden death or successful resuscitation of ventricular fibrillation in 10, and ruptured chordae in 12.[10] Of 62 patients with late systolic murmurs, with or without associated clicks, who were initially free of cardiac enlargement and major complications of mitral valve prolapse and were followed for a mean of 13.8 years, 5 developed endocarditis, 2 died of cardiovascular deaths due to endocarditis or progressive mitral regurgitation, and 1 patient required mitral valve replacement for chordal rupture.[51] In another group of 40 patients with midsystolic clicks and late systolic murmurs followed for over ten years, 5 died suddenly and 2 developed congestive heart failure.[57] None developed endocarditis or required mitral valve replacement.[57] Complications were noted by Mills et al in 8 of 53 patients (15 percent) with midsystolic clicks and/or late systolic murmurs followed for a

mean of 13.7 years and included sudden death (1 patient), ventricular fibrillation (1 patient), bacterial endocarditis (3 patients), progressive mitral regurgitation (5 patients), requiring mitral valve replacement in 2 patients, and 1 death secondary to bacterial endocarditis with acute chordal rupture.[59] It is not uncommon for auscultatory findings to change with time. New murmurs or lengthening of prior murmurs frequently develop.[56,57]

Management

The high prevalence of mitral valve prolapse and the rather low incidence of major complications provide a dilemma with regard to patient counseling and therapy. Should patients be told of the risk of sudden death or severe mitral regurgitation when their chance of developing either is small? Should activities be curtailed? Even if antibiotic prophylaxis and anti-arrhythmic prophylaxis were known to be effective in preventing bacterial endocarditis and sudden death, do the risks of prophylactically treating large numbers of patients outweigh the risks of complications which occur in only a small percentage? Can negative inotropic agents, such as propranolol, decrease the rate of progression of valvular damage and prevent the development of severe mitral regurgitation? Further research is obviously needed with regard to the natural history of mitral valve prolapse in symptomatic and asymptomatic patients in order to answer some of these questions. Subgroups at high risk for bacterial endocarditis, sudden death, progressive mitral regurgitation, and/or chordal rupture need to be identified so that carefully controlled trials of the efficacy of medical intervention can be performed.

The following approach can currently be recommended to patients with mitral valve prolapse. The patient should be informed of the presence of a click and/or murmur. Reassurance that the syndrome is generally benign should be offered. Patients should generally not be informed regarding the risk of sudden death, but the physician should emphasize that palpitations, lightheaded spells, and syncope, if they occur, should be brought immediately to the physician's attention. No activity restrictions are necessary unless arrhythmias related to exercise are uncovered. Patients with a history of dizziness, syncope, or frequent palpitations or those in whom multiple premature ventricular contractions are noted on routine electrocardiogram should undergo Holter monitoring and treatment of any identified malignant ventricular ectopic activity. Careful assessment of the response of ventricular ectopic activity to therapy must be performed, with appropriate changes in medication until control of arrhythmias is achieved. Although of unproven efficacy, antibiotic prophylaxis for endocarditis should be given to those patients with a murmur and probably to patients with clicks, unless other contraindications such as allergy to antibiotic exist. Whether prophylaxis is indicated for the auscultatory-silent form of mitral valve prolapse is not known.

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