Mitral Valve Prolapse or, What to Ignore in Cardiology

SUMMARY

The presence of an isolated midsystolic click and/or late systolic murmur in an otherwise healthy young individual is a totally benign entity and represents a normal variation of mitral valve motion and function. There exists a very small subset of patients with mitral prolapse easily identified by certain clinical characteristics, who have distinct pathologic changes in their mitral valve leaflets and supporting structures. (Can Fam Physician 1981; 27:631-634).

SOMMAIRE

La présence d’un claquement mid-systolique isolé et/ou d’un souffle systolique terminal chez un jeune individu par ailleurs en bonne santé, est totalement bénin et représente une variation normale du fonctionnement de la valvule mitrale. Il existe un très petit nombre de patients avec un prolapsus de la valvule mitrale et cette condition est facilement identifiable par certaines caractéristiques cliniques: on note des changements pathologiques distincts dans les piliers de la valvule mitrale et les structures les supportant.

PROLAPSE OF THE mitral valve is a clinical curiosity which unfortunately acquired a notoriety all out of proportion to its benign and trivial nature. It is not surprising that the practicing physician is often in a quandary when faced with a patient having a midsystolic click and/or late systolic murmur. Some published reports will have him believe that mitral valve prolapse is a harbinger of such life-threatening conditions as malignant arrhythmias, infective endocarditis and strokes. Reading further, the physician can easily be persuaded that mitral valve prolapse is structurally linked to a wide range of serious acquired and congenital heart disorders. On the other hand, he may take comfort in the notion that mitral valve prolapse conveniently affords a facile explanation for such perplexing symptoms as chest pains, palpitations, dyspnea, fatigue and light headedness—a constellation of symptoms bearing a striking resemblance to anxiety neurosis or what used to be called neurocirculatory asthenia.

There may be a small kernel of truth to each of these allegations—and so a number of practical questions arise. Is mitral valve prolapse of any clinical significance? If so, how can one identify those patients who may be at risk for any of the complications previously described? Finally, what should the physician tell the patient once mitral valve prolapse is confirmed by either auscultation or echocardiography?

Clinical Characteristics

Until the early Sixties the presence of a midsystolic nonejection click was thought to be of extracardiac origin. Reid1 suspected and Barlow2 later confirmed that the click, with or without a late systolic murmur, was an intracardiac event produced by sudden tensing of the chordae causing a redundant mitral valve to balloon or prolapse. This phenomenon has since been substantiated by ventriculography, intracardiac phonocardiography and, more recently, echocardiography. It happens that patients with this entity often present with nonspecific complaints such as chest pain, fatigue, palpitations and dyspnea. The chest pain is often described as a sharp stabbing left submammary pain which is prolonged and not necessarily related to physical effort, emotional stress or position. Palpitations are often due to sinus tachycardia but can arise from a variety of atrial and ventricular ectopic tachyarrhythmias. Dyspnea and fatigue are common complaints but unassociated with objective evidence of cardiac dysfunction. These symptoms are noticeably rare among those patients in whom mitral valve prolapse is first discovered on a routine physical examination and before the patient is informed of any abnormality. All age groups are affected and although both sexes appear equally involved when examined as part of a random selection of otherwise healthy individuals, the majority of self-referred patients are women aged 20-55.

The diagnosis of mitral valve prolapse is made by typical auscultatory findings or echocardiography. With the patient in the supine position, a high frequency sharp midsystolic sound (click) is heard at the apex or lower left sternal edge. A midsystolic or late systolic crescendo murmur may or may not be present. These sounds can be enhanced or first detected under
Prevalence is unknown. 

Report prevalence rates ranging from five to 20% of the adult population. Why is there such disparity? 

There are several reasons. First, as indicated above, the condition is evanescent and yet very few studies have insisted on more than one physical examination to establish the diagnosis. Second, the chance of a positive diagnosis seems directly related to the zeal of the authors’ search for positive findings. 

For example, in a recent study, mitral valve prolapse was found in only four of 100 randomly selected male medical students. Although auscultation was performed on these subjects in the upright as well as supine positions, neither the Valsalva manoeuvre nor pharmacologic interventions were employed. In another study of 107 medical housestaff, the auscultatory criteria included separate physical examinations by two different physicians. Subjects were examined in the sitting, supine and standing positions, as well as pre- and post-Valsalva. A diagnosis was established by either auscultation or echocardiography. Ten percent of these subjects had midsystolic clicks and seven percent had unequivocal evidence of mitral valve prolapse by any of the standard criteria. Finally, in a detailed study by Marcewicz et al, 100 presumably healthy young females aged 17-35 were examined in the supine, left lateral and standing position as well as following amyl nitrate inhalation. There was a 17% incidence of prolapse using phonocardiograms and a 21% incidence with echocardiograms. Only eight of 17 subjects had auscultatory evidence of a midsystolic click in the standard supine position while the remaining nine, or greater than 50% of subjects, had auscultatory evidence of prolapse when examined under conditions which exaggerated the reduction in left ventricular filling volume. Also, 42% of their subjects had a systolic murmur heard on routine examination, while 65% had a murmur detected following inhalation of amyl nitrate. 

Clearly therefore, considerable variation of auscultatory and echocardiographic findings occur depending on the position of the patient and the circulatory dynamics, as well as such technical factors as the position and angle of the transducer. One can only conclude from these studies that the true prevalence of mitral valve prolapse has yet to be found and, judging from the limited criteria used thus far, the prevalence rate probably exceeds 20% of the adult population. Can a condition so common in the general population be potentially harmful? 

In the early literature we were besieged by ominous reports of malignant arrhythmias, sudden death and infective endocarditis directly attributed to mitral valve prolapse. These reports originated from tertiary specialty centres with their selected case referrals. As more patients were followed prospectively, it became clear that mitral valve prolapse was a very common and benign entity. Prognostic data have been derived mostly from retrospective analysis and are thereby subject to basic flaws in epidemiological design. Craig in 1977 examined the natural history of mitral valve prolapse in 53 patients over a ten year period. 

This was a retrospective study based upon original phonocardiographic evidence of a click and/or systolic murmur. The inception cohort or characteristics of the entry group were not fully defined and the patients were selected from a tertiary referral practice. No adjustment was made for concurrent illness or other prognostic factors and no objective criteria were given as to the reliability of the phonocardiographic diagnosis. Craig found only two deaths over a ten year period in which prolapse could be causally implicated. 

However, until such time as a careful prospective study is undertaken on a randomly selected ‘healthy’ population or one originating from a primary health care source, the natural history of mitral valve prolapse will remain uncertain. And yet, on the basis of our knowledge thus far, it is safe to assume that life expectancy for the vast majority of subjects with the incidental finding of mitral prolapse is no different from the general population. What then of those sinister associations and complications ascribed to mitral valve prolapse? 

Clinical Associations and Complications 

It is hardly surprising that a clinical entity as common as mitral valve prolapse should be implicated in a variety of cardiac diseases. Indeed, it is now official that mitral valve prolapse has been associated with every known ac-
quired and congenital cardiac disorder. However, there appears to be a more frequent association with those cardiac lesions in which the left ventricular cavity is either normal or reduced in size. For example, mitral valve prolapse is said to occur in more than 20% of patients with atrial septal defect of secundum type. It is not uncommon in patients with muscular subaortic stenosis, coronary artery disease, Wolff-Parkinson-White syndrome, hyperadrenergic states and certain high output conditions such as thyrotoxi-
cosis.8, 9 Tricuspid valve prolapse is not uncommon in certain forms of Ebstein’s anomaly where the right ventricle is vestigial in proportion to the size of the tricuspid valve. Conversely, it is rare to find mitral valve prolapse in advanced conditions of volume loading such as congestive cardiomyopathy, aortic valvular insufficiency and extensive myocardial infarction with left ventricular aneurysms.

How can we reconcile the ominous complications attributed to mitral valve prolapse with what otherwise appears to be a trivial lesion? The original reports of sudden death in patients with mitral valve prolapse have proven to be exaggerated. On careful analysis, most of those patients who died suddenly showed evidence of either severe mitral regurgitation or serious arrhythmias often associated with such electrophysiologic disturbances as prolonged QT intervals or Wolff-Parkinson-White syndrome. Similarly, the incidence of infective endocarditis in patients with mitral prolapse is not as frequent as previously believed. Most cardiologists would now agree that the presence of a click alone does not constitute a requirement for prophylactic antibiotics. On the other hand, any suspicion of distinct valvular pathology such as echocardiographic evidence of holosystolic prolapse, thickening of leaflets or annulus or increased left atrial size would be sufficient to recommend antibiotic prophylaxis in the event of dental and other instrumentation procedures.

Arrhythmias are common in patients with mitral valve prolapse but they are also common in the general population if one is diligent enough in one’s search. The approach to arrhythmias depends upon the nature of the arrhythmias, the presence or absence of an underlying electrophysiologic or organic disorder and to what extent the arrhythmia is interfering with the patient’s wellbeing. Patients with the prolonged QT syndrome, WPW, symptomatic coronary artery disease and hemodynamically significant mitral valve reflux constitute a very small percentage of patients with prolapse. They are at risk of developing more serious arrhythmias and should be considered for antiarrhythmic therapy. Beta blockers have been found to be a well tolerated and effective means of therapy for frequent ventricular ectopic activity and atrial tachyarrhythmias.

Finally, mitral valve prolapse has been implicated in systemic thromboembolic conditions such as cerebrovascular accidents. Barnett found that out of 166 patients who suffered a stroke, 12 had mitral prolapse.10 Others have also suggested a greater than normal incidence of prolapse among patients with transient ischemic attacks; some authors have even demonstrated abnormal platelet function in patients with mitral prolapse.11 The notion that mitral prolapse may be a source of systemic emboli has been challenged recently by reports demonstrating a poor correlation between strokes and mitral valve prolapse among groups of consecutive patients with acute cerebrovascular events.12 Furthermore, attempts to find an embolic source in the heart have met with consistent failure—unless there was coexisting organic cardiac disease, cardiomegaly or atrial fibrillation.

Pathology

The textbooks describe mitral valve prolapse as a structural rather than functional entity characterized by myxoid degeneration and myxomatous proliferation of the valve leaflets and supporting structures. From surgical and autopsy material, one may see pathologic changes beginning with the spongiosa component of the valve which then proliferates and lays down increasing concentrations of acid mucopolysaccharide, presumably due to a basic defect in collagen metabolism. As the disease progresses there is myxomatous proliferation in the valve leaflets, chordae and annulus with degeneration of collagen leading to redundant cusps, mitral regurgitation, annular calcification and possibly chordal rupture.

How does one equate these rather formidable pathologic changes with the high prevalence of this entity in an otherwise healthy population? Is it possible that one out of every four of us is walking about with these progressive, destructive changes in our mitral valve? Hardly so. In fact, if we peered in from the pathologist’s vantage point we would find non-rheumatic deformity of the mitral valve occurring in less than five percent of routine autopsies. In a recent series of 294 consecutive post mortem examinations, the incidence of floppy or ballooning mitral valves secondary to pathologic changes constituted less than five percent; no one under 40 years of age had any histologic abnormality of the valve.13

What does this mean in the light of the high clinical prevalence of the entity? There are three possibilities. Subjects with mitral valve prolapse are immortal and 80% of them either never die or are never examined post mortem. Second, all patients with prolapse have distinct pathologic changes which miraculously disappear prior to death. It is clearly less absurd to accept the third notion that the vast majority of patients with clinical or echocardiographic evidence of prolapse have no detectable valve pathology and the auscultatory findings are simply due to changes in motion and function of the mitral valve within a spectrum of normality.

If we consider the intricate and complex arrangement of the mitral valve apparatus and particularly the interlace branching pattern of the chordae tendonea, it is not hard to imagine how slight variations in architecture can produce changes in mitral valve motion under different loading conditions. In a recent report, 36 out of 40 patients with post mortem evidence of ballooning mitral valve displayed small variations in chordal branching patterns compared to only eight percent of those with normal hearts.14

The variation in branching pattern could create an inadequate compensatory support from neighboring chordal structures, thereby causing prolapse when the ventricular volume and hence orientation of subvalvular structures are altered. In this context it is pertinent to recall once again that the success of diagnosing mitral valve prolapse is enhanced the more diligent the effort of the examining physician to reduce the left ventricular volume. This
theory of functional anatomy is also in keeping with the increased incidence of prolapse in those conditions with reduced or normal left ventricular volumes. When volume loading, cardiac dilatation and congestive heart failure occur in association with mitral valve prolapse, there is usually evidence of definite pathologic deformity of the valve as described above.

**Conclusion**

If mitral valve prolapse is discovered on a routine examination of an otherwise healthy adult, the physician should regard it as a completely benign entity and every attempt made to reassure the patient that no cardiac abnormality exists. At the same time, the physician should be alerted for the small subset of patients in whom significant mitral regurgitation occurs or, because of certain characteristics such as connective tissue disease and thoracic skeletal deformities, the prolapse may be due to pathologic changes in the valve. Patients with holosystolic murmurs and marked scalloping, thickening or calcification of the valve or annulus should be considered for further investigation and therapy. Beta blockade can be effective in patients with annoying and frequent arrhythmias, particularly in those in whom the arrhythmia is heightened during states of adrenergic stress. There is no evidence that prophylactic antibiotics are of any use in patients with an isolated midsystolic click or late systolic murmur. However, prophylaxis is urged in those cases with either holosystolic prolapse or distinct valvular incompetence. The association of transient cerebral ischemic attacks with mitral valve prolapse is an unresolved issue. A young patient with mitral valve prolapse who suffers either a stroke or unexplained transient ischemic attacks should be considered for further cardiac investigation and, possibly, antiplatelet therapy.

The tertiary specialist should be encouraged and supported to continue unraveling the secrets of the mitral valve and expand our knowledge of this clinical entity. On the other hand, he should be cautioned against premature or generalized pronouncements based upon highly selected case referrals. There have been no less than 700 citations on mitral valve prolapse in the English language literature. So far, none of these papers nor any textbook on mitral valve prolapse has devoted a chapter or section to the psychological impact of the diagnosis on the patient. This might prove to be the most fruitful area for future studies. It is prophetic that in the past two years, the purely descriptive studies on mitral valve prolapse are being gradually replaced by a burgeoning psychiatric literature pertaining to a clinical phenomenon which, in the final analysis, may prove to be nothing more than a curious motion artifact of an otherwise healthy valve.

**References**


**Recommended starting dose**, 20 mg q.i.d.

**INDICATIONS**

In peripheral vascular disorders: For relief of symptoms such as intermittent claudication, coldness, numbness, pain and cramping of the extremities—in the management of arteriosclerosis obliterans, diabetic vascular diseases, thromboangitis obliterans (Buerger's disease), Reynaud's disease, postphlebitic conditions, acroparesthesia, frostbite syndrome and ulcers of the extremities (arteriosclerotic, diabetic, va."

**CONTRAINDICATIONS**

VASODILAN should NOT be used in the presence of arterial bleeding or immediate postpartum.

**SIDE EFFECTS**

Few side effects have been observed with recommended oral doses. Occasional transient palpitation or dizziness may occur, but these can be controlled by dosage reduction.

An intramuscular dose of 10 mg may result in hypotension and tachycardia. These symptoms are more pronounced at higher doses. For this reason, intramuscular doses exceeding 10 mg are not recommended. Repeated intramuscular administration of 5 to 10 mg at suitable intervals may be employed.

**PRECAUTION**

In the presence of pre-existing hypotension or tachycardia, intramuscular administration should be used with extra care and the patient should be observed closely. Intravenous administration is not recommended for peripheral vascular disease because of the increased likelihood of side effects.

**DOSEAGE AND ADMINISTRATION**

In peripheral and cerebral vascular disorders:

Oral dosage: 20 mg t.i.d. or q.i.d. for at least 21 days. Subsequent dosage may be adjusted to individual patient response. Intramuscular dosage: 5 to 10 mg (1 to 2 ml) two or three times daily. Intramuscular administration may be used in the initial treatment of acute and severe symptoms. As these symptoms are controlled, the patient may be maintained on oral therapy.

**AVAILABILITY**

Tablets 20 mg (blue)—bottles of 50 and 250. orally (white)—bottles of 100 and 500.

Ampoules: Injectable 5 mg per ml—8 ml and 20 ml ampoules—boxes of 24.

**Full prescribing information available on request.**

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