Mitral valve prolapse
its relevance in general practice

Important issues in patients with mitral valve prolapse include bacterial endocarditis prophylaxis when there is mitral regurgitation and closer surveillance of patients who are aged 50 years and older.

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Mitral valve prolapse (MVP), or 'floppy mitral valve', is usually a benign anatomical variant that occurs in about 3% of the adult population. It was first identified as an entity some 40 years ago and since that time there have been a number of misconceptions about it. However, during the last 10 or so years a clear picture of the relevance of the diagnosis has emerged, and the management of complications has become well defined in the small subset of patients in which they occur. Associations with relatively uncommon genetic disorders have also been identified.

Valve anatomy in MVP

As shown in Figure 1, the variant valve in MVP tends to have disproportionately long chordae tendineae and large diameter leaflets. As a consequence, during systole there is a protrusion of one or both mitral leaflets by 2 mm or more beyond the atrioventricular groove and into the left atrial cavity. If only one leaflet is involved, it is more commonly the posterior leaflet. Leaflet displacement may be associated with an increase in leaflet thickness of up to 5 mm.

Using current M-mode and two-dimensional echocardiography with Doppler studies, increased thickness (by up to 5 mm) of the prolapsing leaflets can be identified in about half of patients with MVP. Thickening of the valve leaflets is associated with myxomatous change. As a group, patients with thickened valve leaflets are more likely to develop marked regurgitation and other complications after the age of about 50 years.

MVP is uncommon in childhood; the changes in the valve tend to emerge in adulthood during and after the growth spurt of adolescence.

Presentation and diagnosis

As MVP is usually a benign variant of normal, in most patients the diagnosis is made incidentally during a routine examination or because of the occurrence of occasional mild palpitations.

Patients tend to be slim and the cardiovascular examination is unremarkable apart from the presence of an isolated nonejection click at the left

IN SUMMARY

- **Mitral valve prolapse (MVP) is characterised by an early systolic click, with or without a late systolic murmur.**
- **It is present in about 3 to 4% of the adult population and is largely benign.**
- **The diagnosis is confirmed by echocardiography.**
- **When a patient has a systolic murmur of mitral regurgitation, antibiotic prophylaxis is indicated for tooth extractions and surgical procedures.**
- **The principal complications of MVP occur infrequently, and usually after the age of 50 years. They include progressive mitral regurgitation, chordal rupture, atrial fibrillation and bacterial endocarditis.**
- **Mitral valve repair is usually indicated only for severe mitral regurgitation.**

sternal edge or in the mitral area, with or without a late systolic murmur. In the more obvious cases in which there is significant mitral regurgitation, the mitral systolic murmur then becomes progres - sively longer and eventually full length. The click, if present, is heard in early systole, and is due to closure of the somewhat larger than usual mitral valve leaflets. Patients often have normal blood pressures, or perhaps even lower than average blood pressures. The electrocardiogram is usually normal or with just an occasional late cycle ectopic beat. An echocardiogram confirms the diagnosis: it identifies the displacement of one or both mitral leaflets beyond the atrioventricular groove and into the left atrium (see Figure 1), and also documents the presence and extent of any jet of mitral regurgitation.

Reassuring the patient that the finding is a mild variant of normal and usually of benign nature is important. However, in view of the family associations and genetic considerations associated with MVP, it is also important to establish whether the diagnosis has been made in other family members. In particular, it should be determined whether affected family members have had complications such as severe regurgitation, need for surgery or, very rarely, sudden cardiac death.

Complications

Although MVP is benign for the most part, there are several recognised and important complications, and these are more prevalent with advancing age and in men. These complications are:

- benign arrhythmias
- atrial fibrillation
- chordal rupture
- myxomatous change and progressive mitral regurgitation
- infective endocarditis
- sudden cardiac death (very rarely).

Population surveys of MVP prevalence using echocardiographic criteria have established that MVP is more common in women than in men – prevalences are about 4% and 3%, respectively. Despite the prevalence difference, both progressive mitral regurgitation with or without chordal rupture and infective endocarditis are about twice as common in men as in women, and are more common with advancing age.

Some years ago, my colleagues and I calculated the lifetime risk for men and women with MVP in New South Wales of developing serious mitral regurgitation requiring valve surgery. In men, the risk was less than 5%, and in women, less than half that ($p<0.001$), with minimal risk before the age of 50 years and a steep increase thereafter.[1] There have been similar results reported from the Mayo Clinic. We also showed that the development of infective endocarditis is age-related, the risk in men is about twice that in women and the risk is associated with concomitant mitral regurgitation.

Mitral valve prolapse

Mitral valve prolapse is relatively common and usually a benign anatomical variant of normal. Complications that may develop include progressive mitral incompetence and bacterial endocarditis. The illustration depicts mitral regurgitation during left ventricular contraction of the heart.

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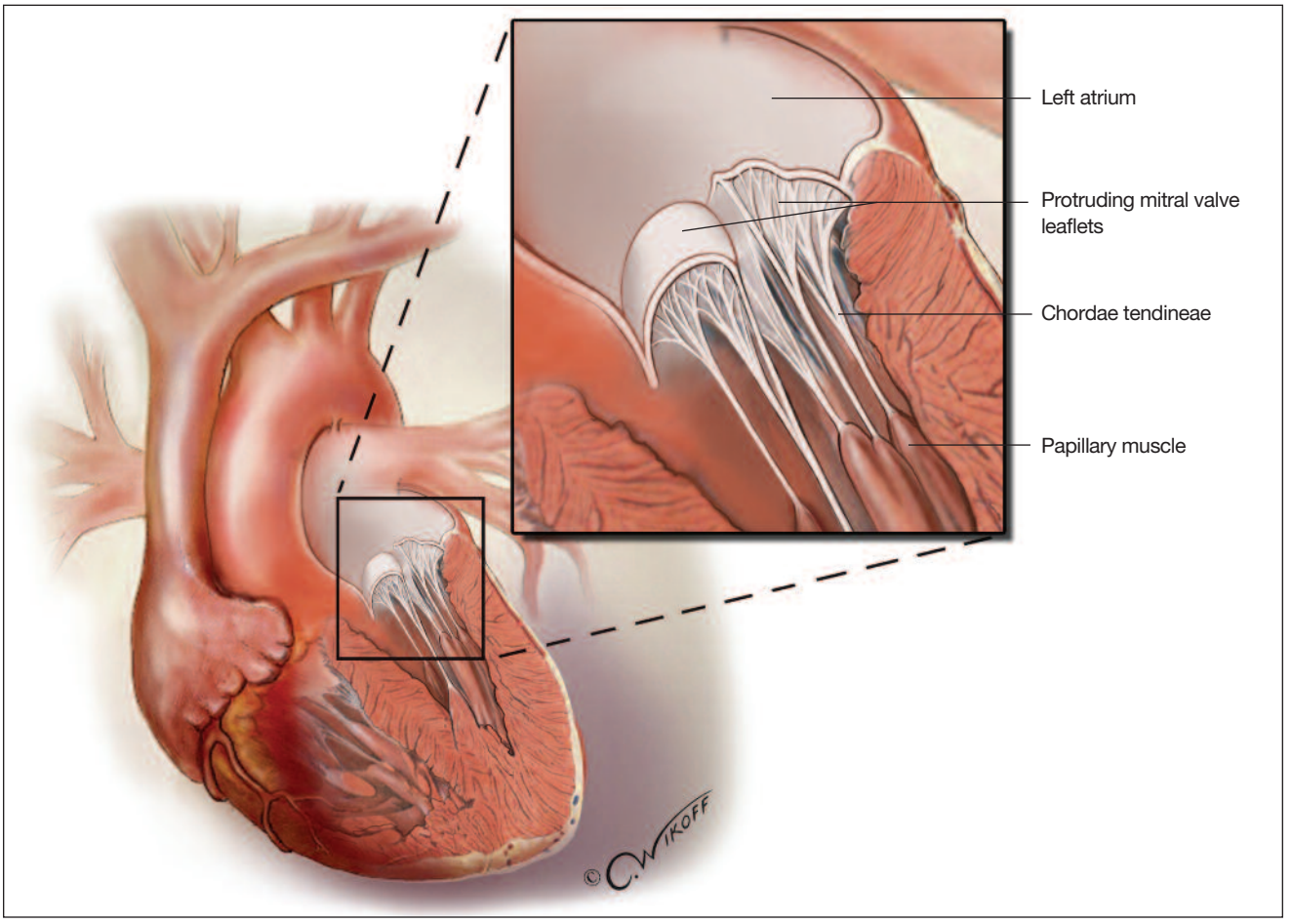


Figure 1. Mitral valve prolapse. There is protrusion of both mitral leaflets into the left atrium, more marked with the posterior leaflet.

We can only speculate on the reasons for the gender differences. Possibly the generally higher levels of physical activity and blood pressure in men compared to women could together impose greater forces on the large volume, prolapsing valve and increase the likelihood of repeated minor repetitive cyclical valve injury.

Geometry and MVP pathogenesis

In an average human lifespan the mitral valve opens and closes more than three billion times. The valve leaflets must withstand the full force of ventricular contraction during each closure period. It has also been shown that the intraventricular force is normally applied unevenly and that the posterior leaflet receives a proportionately greater force because of the normal orientation of the valve leaflets. A pattern of repeated minor injury with greater effect on the posterior leaflet may result.

In a valve with anatomical variation, the stretch, physical tension and pressure alterations resulting from the variation and the 'normal' uneven intraventricular forces together, over many years, contribute in a major way to the development of myxomatous change and ultimately to significant valve incompetence (see the flowchart on page 15).[1,2]

Family associations and genetic disorders

There is some aggregation of MVP within families. We studied 206 first degree relatives of 65 patients with MVP. In 21 (10%) of the first degree relatives there was also MVP; however, not one of these identified MVP subjects was aware of the cardiac findings at the time.[3]

We also assessed first degree relatives of patients who had come to surgery for severe mitral regurgitation due to a myxomatous valve, and compared the findings with those in 320 age- and sex-matched healthy controls.[4] Whereas 3.5% of the controls had MVP as expected from the population prevalence, in the first degree relatives of the patients who had come to surgery 20% had MVP ($p<0.001$). These were a select, severely affected, patient group. From our data overall, the first degree relatives of the

subjects with MVP were about 2.5 times more likely to also have MVP than were age-matched healthy controls. These findings are consistent with a polygenic pattern of inheritance in which there is a variable degree of penetrance.

We also conducted collagen studies, in which we obtained normal mitral valves at postmortem and compared the biochemical changes with those in myxomatous mitral valves removed at surgery because of severe mitral regurgitation. In the myxomatous valves there was an increase in type III collagen and mucopolysaccharide;[5] recently, increased fibrillin-1 has also been identified in these valves.[2] We believe that these changes result from repetitive minor valve injury.

In relation to genetic aspects, it is worth recalling that the two most common dominantly inherited disorders in which there is a high incidence of MVP are Marfan's syndrome and hypertrophic cardiomyopathy. In Marfan's syndrome, which has a prevalence of one in 5000 in the Caucasian population, about 80% of cases have MVP. Hypertrophic cardiomyopathy is 10 times as common, and here too, MVP is not infrequent.

There is also the occasional family in which, although there does not appear to be a well defined genetic disorder, dominantly inherited MVP is occurring – often with sinister complications. The pattern of inheritance in such a family is shown in the box on page 16.

To summarise, the available evidence suggests that familial aggregation of MVP among most people with MVP is due to polygenic inheritance. Our data would suggest that the likelihood of a first degree relative of an MVP patient having MVP is about 2.5 times the population average. There is an increased prevalence in some dominantly inherited genetic disorders, such as Marfan's syndrome and hypertrophic cardiomyopathy, and the rare occurrence of dominantly inherited MVP with mitral regurgitation and increased risk of potentially lethal cardiac arrhythmias.

Management

Uncomplicated cases

Patients identified incidentally as having MVP who do not have relevant family histories and are asymptomatic simply require reassurance and review at about three-yearly intervals. Those with any degree of mitral regurgitation should be advised about the need for antibiotic prophylaxis for bacterial endocarditis.

The American Heart Association recommends endocarditis prophylaxis when undergoing invasive procedures for patients with MVP who have some associated mitral regurgitation, but not for those without valvular regurgitation as their risk is minimal.[6]

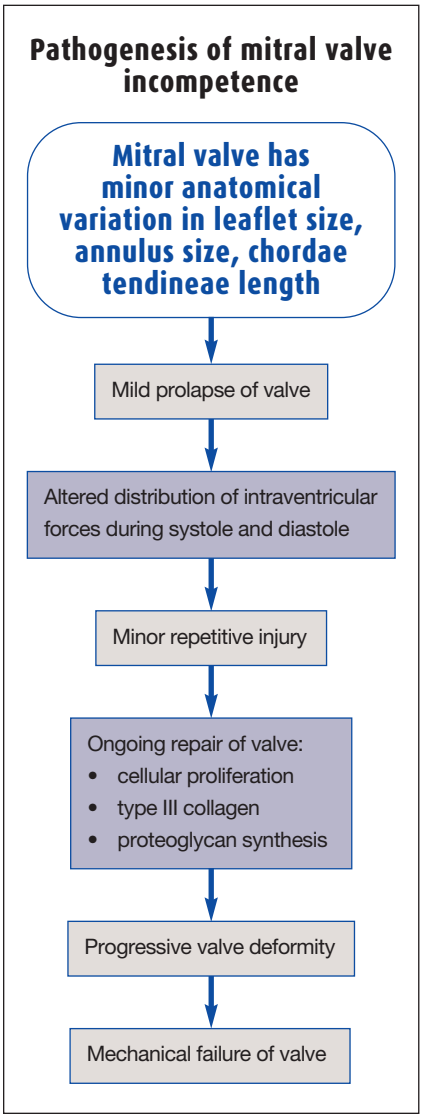
For dental procedures, endocarditis prophylaxis is a single dose of amoxycillin, 2 g for an adult, an hour before the procedure. For individuals allergic to penicillin, clindamycin (Cleocin, Dalacin-C) in an effective equivalent dose can be offered.

For gastrointestinal or genitourinary procedures, oral amoxycillin 2 g one hour before the procedure or intramuscular or intravenous ampicillin (Aspen Ampicyn, Austrapen, Ibimycin) 2 g within 30 minutes before starting the procedure is recommended. For patients allergic to penicillin, intravenous vancomycin (Vancocin, Van - comycin Hydrochloride for Intravenous Infusion) 1 g over a one-to two-hour period should be given and completed about 30 minutes before the start of the procedure.

Regarding pregnancy, well documented cases of endocarditis after a normal vaginal delivery are uncommon and, therefore, antibiotic prophylaxis for a normal vaginal delivery is not recommended.[6]

Cases with complications

Severe mitral regurgitation requiring surgery is uncommon before the age of 50 years. As previously mentioned, although the prevalence of MVP tends to be greater in women, the development of severe mitral regurgitation requiring surgery occurs more commonly in men. If surgery is needed, repair of the valve is usually possible, rather than replacement. From our prevalence data, by the age of 70 years, about 4% of men and 2% of women with classic MVP will require mitral valve surgery.[1] However, frequencies of about twice these have been quoted by others.[2] Surgery may be required relatively acutely because of rupture of chordae tendineae and sudden exacerbation of mitral regurgitation



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Dominant inheritance of MVP

The dominant inheritance of MVP in three generations of a family is illustrated in the Figure. The affected members of this family had significant mitral regurgitation and potentially fatal ventricular arrhythmia.

In the first generation, the mother died at the age of 65 years following mitral valve surgery for myxomatous valve disease. In the next generation, both sons had MVP with mitral regurgitation. One son died suddenly at the age of 28 years, and the diagnosis of MVP with myxomatous change was confirmed at autopsy; his son also has MVP. In the other son of the second generation, there was documented MVP with moderately severe mitral regurgitation. At the age of 43 years, he suffered a cardiac arrest, with successful resuscitation. Subsequent angiography revealed normal coronary arteries, and an electrophysiological study documented inducible ventricular tachycardia that was prevented by sotalol. He remains well after mitral valve replacement and while continuing twice daily sotolol.

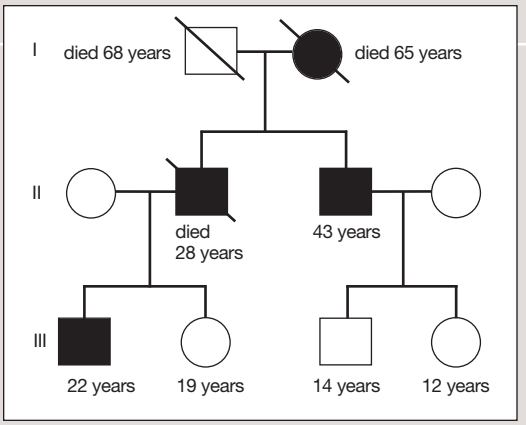

Figure. Dominant inheritance in MVP with myxomatous valve change.

because of the flail mitral leaflet.

Patients who have significant mitral regurgitation and left atrial dilatation often develop atrial fibrillation. In those who, for medical or other reasons, are not recommended for surgery, there is a requirement for long term anticoagulation because reversion to sinus rhythm is unlikely in these patients. In the occasional patient in stable sinus rhythm, transient ischaemic attacks may occur in the absence of carotid disease; long term low dose aspirin (Astrix, Cardiprin 100, Cartia) therapy is recommended for these patients.

Sudden cardiac death due to ventricular fibrillation is a rare complication and is almost always associated with significant mitral regurgitation. In patients who survive ventricular fibrillation, surgical repair or replacement of the valve is essential. An electrophysiological study should be performed before surgery and appropriate antiarrhythmic therapy continued thereafter, usually with sotalol (Cardol, Solavert, Sotacor, Sotahexal). Careful family studies are mandatory in this very uncommon situation, and an appropriate prophylactic regimen should be implemented for any family member identified as having MVP.

Conclusion

MVP is relatively common and is usually a benign anatomical variant of normal. Complications, while uncommon, are more frequent in men and with advancing age. They include the development of progressive mitral incompetence and bacterial endocarditis. The important management strategies are bacterial endocarditis prophylaxis when a patient has mitral incompetence and close surveillance in patients aged 50 years and older because a small but significant number will develop progressive mitral regurgitation and require surgical repair of the valve.

MVP has a genetic component, with about 10% of first degree relatives affected. There are also some connective tissue disorders, particularly Marfan's syndrome and hypertrophic cardiomyopathy, in which MVP is frequent. MT

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DECLARATION OF INTEREST: None.

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