The clinical and diagnostic features of mitral valve disease

John Chambers

Mitral valve disease remains common, and requires regular clinical and echocardiographic review. Surgery is indicated soon after the development of symptoms or at the first sign of left ventricular decompensation in mitral regurgitation or of the right ventricle in mitral stenosis.

Mitral valve disease has not been relegated to the history books with the decline in rheumatic disease in the West. In the USA in 1994, 422 000 patients received a discharge diagnosis of mitral valve disease, as many as one half the number with acute myocardial infarction (Anon, 1995).

The mitral apparatus consists of the valve itself, but also the annulus, chordae, papillary muscle and the adjacent myocardium. Dysfunction of any or all of these can cause mitral regurgitation. The most common causes leading to surgery are ischaemic regurgitation, prolapse and endocarditis. Mitral stenosis is less common, accounting for 9% of valve disease (Horstkotte et al, 1991). It is almost invariably rheumatic in origin although rare congenital causes exist (*Figure 1*).

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MITRAL REGURGITATION

Symptoms and natural history

The mortality in severe mitral regurgitation of all aetiologies with and without symptoms is around 5% per year (Delahaye et al, 1991). The natural history of mitral regurgitation secondary to left ventricular dysfunction largely reflects the underlying condition. However, the presence of moderate or severe regurgitation may independently worsen the prognosis thus justifying repair (Chen et al, 1998).

Chronic severe mitral regurgitation as a result of primary valve dysfunction causes dilatation and hyperactivity of the left ventricle. Long-term volume load induces myocardial fibrosis with a consequent deterioration in contractile function. However, because the left ventricle is emptying partly into the left atrium which is at a far lower pressure than the aorta, the left ventricular ejection fraction or fractional shortening is apparently normal until the terminal stages (Corin et al, 1995).

Severe mitral regurgitation may be asymptomatic (Delahaye et al, 1991) or may cause exertional breathlessness and orthopnoea. Exercise testing should be considered in any patient who claims to be asymptomatic and in whom the history is less than clear. Left atrial enlargement secondary to the mitral regurgitation is associated with paroxysmal or sustained atrial arrhythmias and if these are present there is an increased risk of thromboembolism for which anticoagulation with warfarin should be considered. Chronic mitral regurgitation is the underlying cause in between 20 and 30% of cases of infective endocarditis (Otto, 1999).

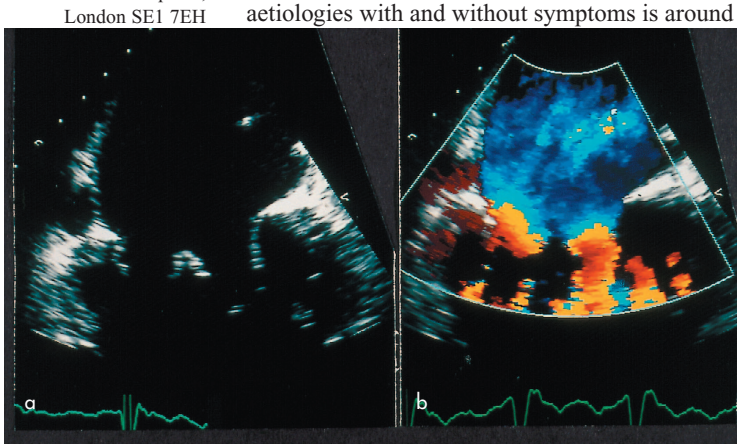

Figure 1. Double orifice mitral valve. This is an uncommon congenital cause of mitral stenosis or regurgitation. This transoesophageal image shows (a) the two orifices and (b) two columns of forward flow during diastole.

Signs

The radial pulse is usually normal, although in severe chronic regurgitation there may be atrial fibrillation. The blood pressure may be low and the carotid upstroke of low volume in advanced disease, but these signs are not specific. The

jugular venous pulse is usually normal since severe pulmonary hypertension leading to right ventricular dysfunction is rare. There may be a parasternal impulse as a result of left atrial enlargement (Basta et al, 1973) and in severe regurgitation the apex is displaced laterally. On auscultation with the bell, there is a pansystolic murmur (*Figure 2b*) at the apex radiating to the axilla. The amplitude is approximately related to the grade of regurgitation (Desjardins et al, 1996), but better indicators of severe regurgitation are a diastolic sound and wide splitting of the second heart sound. The diastolic sound is composed of a third heart sound sometimes succeeded by a mid-diastolic murmur caused by

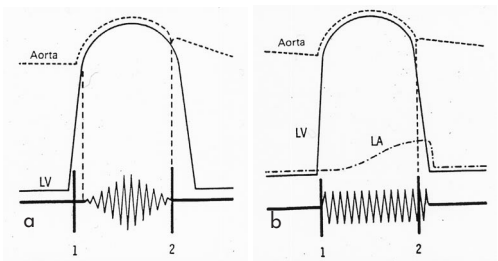

Figure 2. The murmurs of mitral regurgitation and aortic stenosis. a. The second heart sound occurs as the aortic valve shuts when the left ventricular pressure falls below aortic pressure. The murmur of aortic stenosis finishes before the second sound. b. The left ventricular pressure continues falling and the mitral valve opens when this pressure falls below left atrial pressure. The murmur of mitral regurgitation therefore continues beyond the second heart sound. From Leatham and Leech (1983). LA= left atrial pressure; LV = left ventricular pressure.

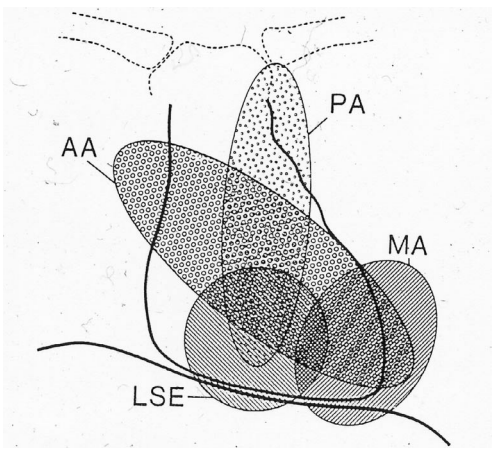

Figure 3. Sites of maximum amplitude of murmurs. The murmur of aortic stenosis may be best heard at the apex and this may lead to confusion with mitral regurgitation. However, the diagnosis should be obvious based on the carotid upstroke and apex beat. The quality of the murmurs is also different. From Leatham and Leech (1983). AA = aortic area; LSE = left sternal edge; MA = mitral area; PA = pulmonary area.

functional mitral stenosis as a result of high flow. The wide splitting of the second sound is caused by early cessation of systole leading to an early aortic closure sound.

It is often thought that the murmur of mitral regurgitation obscures the second sound but this is not true. The murmur does, however, continue beyond the second sound which is in contradistinction to the situation in aortic stenosis (*Figure 2a*). It is easy to mistake the murmurs of aortic stenosis and mitral regurgitation. The ejection systolic murmur of aortic stenosis may only be heard at the apex (*Figure 3*), but it finishes before the second sound and is also harsher in quality. Furthermore, the carotid upstroke is usually slow and the apex undisplaced in severe aortic stenosis in the presence of preserved left ventricular systolic function. If the mitral regurgitation is mild and caused by prolapse, there may be a late systolic murmur sometimes preceded by a systolic click (*Figure 4*). The eccentricity of the jet may cause unusual radiation of the murmur to the base of the heart or even to the back or carotid artery (Antman et al, 1978).

Assessment

Echocardiography confirms the diagnosis by the presence of reversed systolic flow in the left atrium. The severity is graded by a combination of factors including the width of the colour jet (*Figure 5*), the size of the flow acceleration in the left ventricle, the pattern of flow in the pulmonary veins, the density and shape of the continuous wave signal and the size and activity of the left ventricle (*Table 1*).

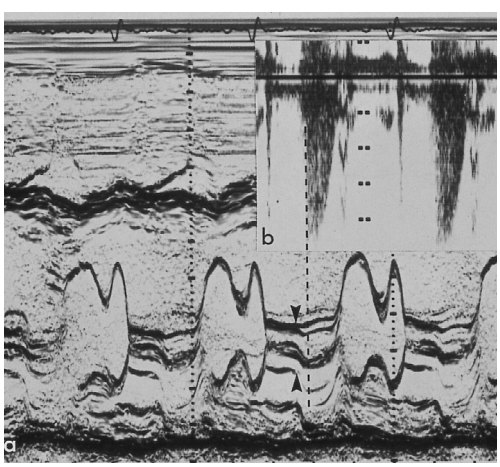

Figure 4. Mitral prolapse. The M-mode shows bowing of the leaflets (arrowed) in the latter half of systole. Regurgitation develops at the time of maximum prolapse as shown by the continuous wave Doppler signal. On auscultation, there was a midsystolic click followed by a crescendo systolic murmur.

The aetiology can be determined from the appearance and motion of the valve and chordae and from the function of the left ventricle. Mitral regurgitation in the West occurs most frequently as a result of left ventricular dysfunction leading to displacement of the papillary muscles or myocardial infarction leading to restriction of the posterior mitral leaflet (*Figure 6*). The most common valvar cause of regurgitation is prolapse (which may also affect the chordae and annulus)(*Figure 5*). Other valvar causes are endocarditis, rheumatic fever, lupus, radiation, the anorectic drugs phentermine and fenfluramine, congenital disease or more rarely trauma or carcinoid syndrome. Hypertrophic cardiomyopathy can cause mitral regurgitation as a result of both abnormal papillary muscle function and an abnormally long anterior leaflet. The echocardiogram shows if mitral valve repair is possible, for example if there is prolapse of the middle portion of the posterior leaflet or significant regurgitation secondary to an inferior infarct (*Figure 6*).

The assessment of the left ventricle is important. When the fractional shortening falls to about 29% or the ejection fraction to about 60%, both at the lower limit of normal, myocardial fibrosis is already at an advanced stage and full recovery after surgery almost never occurs (Enriquez-Sarano et al, 1994). Surgery should therefore be considered in an asymptomatic patient aged under 70 years at the first sign of end-systolic dilatation, for example to an M-mode dimension of 4.0–4.5 cm (Wisenbaugh et al, 1994). After this point there is a rapid deterioration and if surgery is delayed until the end-systolic dimension is > 5.0 cm, all patients either die or remain in heart failure (Wisenbaugh et al, 1994). For patients aged over 70 years the risk of surgery is higher and surgery is usually recommended only for symptoms (Bonow et al, 1998).

TABLE 1.
Guidelines to grading mitral stenosis

	Mild	Moderate	Severe
Orifice area (cm^2)	> 1.5	1.0–1.5	< 1.0
Pressure half-time (ms)	< 150	150–200	> 200
Mean gradient (mmHg)	< 5	5–10	> 10

Cardiac catheterization is not usually necessary unless there are discrepancies between the echocardiographic and clinical features. The grade of regurgitation can be judged from the density and speed of opacification within the left atrium after a left ventricular injection of contrast. The height of the V wave on the pulmonary wedge pressure trace is also a guide, but is non-specific since it also occurs in conditions associated with delayed left atrial emptying (Fuchs et al, 1982).

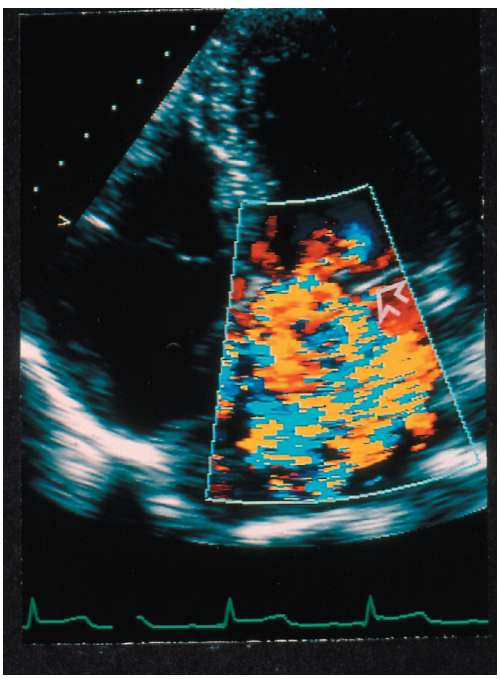

Figure 5. Severe mitral regurgitation on colour mapping. The cause was prolapse of the posterior leaflet (arrowed).

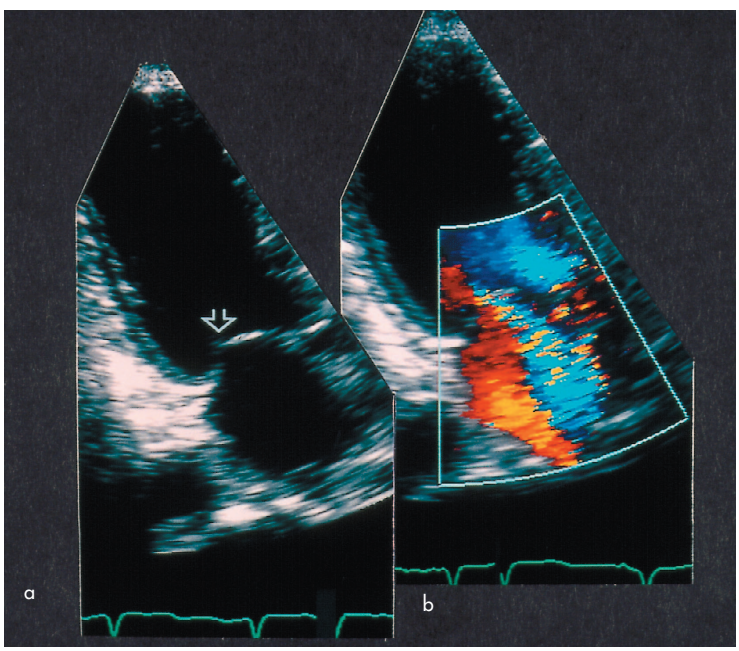

Figure 6. Ischaemic mitral regurgitation. There is an inferior infarct. This means that the inferior wall cannot shorten during systole so that the inferomedial papillary muscle stays at a distance from the mitral annulus. a. The posterior mitral leaflet is, therefore, held within the left ventricle and fails to move back level with the annulus. b. This causes posteriorly-directed regurgitation. Repair with an annuloplasty ring is usually possible.

MITRAL STENOSIS

Symptoms and natural history

The normal mitral orifice is 4–5 cm^2 in area and symptoms do not occur until the orifice area falls to below about 2.0 cm^2. The rate of haemodynamic progression may be very slow in about two-thirds of patients, but in those with more calcified and deformed valves the decrease in orifice area may be as high as 0.3 cm^2 per year (Gordon et al, 1991). In one study, symptoms developed 16 years after the acute illness and become severe after a further 9 years (Horstkotte et al, 1991). The 5-year survival with severe symptomatic mitral stenosis is 44% without surgery (Horstkotte et al, 1991).

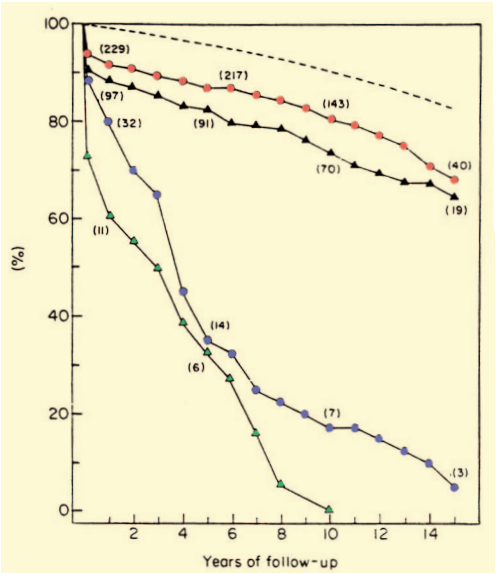

Figure 7. Graph of outcome of asymptomatic compared with symptomatic severe mitral stenosis. Survival of patients with isolated mitral stenosis (open circles) or mitral regurgitation (open triangles) in whom surgery was indicated, but who were treated medically. Survival of patients with mitral stenosis (solid circles) or mitral regurgitation (solid triangles) who were treated with valve replacement. The expected survival in the absence of mitral valve disease is given by the upper dashed line. From Horstkotte et al (1991).

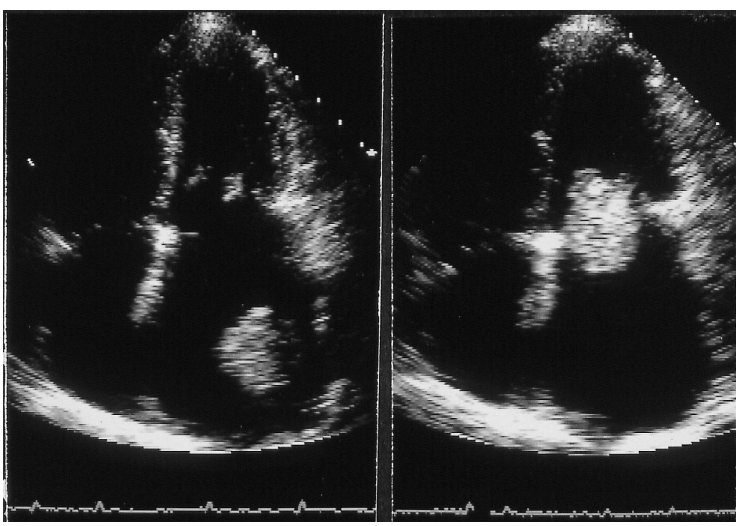

Figure 8. Ball thrombus. This patient with severe mitral stenosis presented with recurrent transient ischaemic attacks despite adequate international normalized ratio levels on warfarin.

The main symptoms are exertional breathlessness as a result of raised left atrial pressure and fatigue as a result of low cardiac output (Rowe et al, 1960). Exertional breathlessness is usually of slow onset so that the patient may claim to be asymptomatic. The presence of symptoms dramatically changes the outcome (*Figure 7*) so, if there is any doubt, the patient should be exercised either formally or by simply walking with them in a hospital corridor. Orthopnoea and paroxysmal nocturnal dyspnoea are caused by the increased venous return on lying down leading to higher left ventricular filling pressures. Recurrent chest infections also complicate chronically elevated left atrial pressure (Wood, 1954).

Pulmonary pressures are raised in mitral stenosis initially by passive back pressure and reactive vasoconstriction. Ultimately histological changes occur similar to those seen in primary pulmonary hypertension and these are irreversible (Otto et al, 1993). In mitral stenosis, the left ventricle is protected since it is downstream from the valve lesion. However, the right ventricle is under threat as pulmonary artery pressure rises. Early right ventricular dysfunction or a rise in pulmonary pressure are therefore criteria for surgery in otherwise asymptomatic severe mitral stenosis (Bonow et al, 1998). Established right heart failure as a result of pulmonary hypertension may cause a reduction in breathlessness as a result of lowered left atrial filling pressures. However, this apparent improvement is spurious and a sign of end-stage and usually inoperable disease.

The risk of thromboembolism in the presence of atrial fibrillation and mitral stenosis is 18 times that of age-matched subjects (Wolf et al 1978) (*Figure 8*) and stroke may be the presenting symptom. Anticoagulation is also recommended in the presence of sinus rhythm and severe mitral stenosis if the left atrial dimension is >5.5 cm (Bonow et al, 1998).

Signs

The pulse is often irregular as a result of atrial fibrillation and the jugular venous pressure may be high. If there is tricuspid regurgitation there will be prominent systolic waves shown as large amplitude waves timed with the central pulse. A malar flush as a result of chronic pulmonary

hypertension is no longer common. As for mitral regurgitation, the carotid upstroke and blood pressure are not specific. There may be a parasternal impulse as a result of dilatation of the right ventricle secondary to pulmonary hypertension. The left ventricle may then be displaced but, on palpation, there should be a still region between the right and left ventricular impulses. In mitral stenosis uncomplicated by right ventricular dilatation, the apex beat is not displaced. The character of the apex is almost invariably normal and the tapping caused by palpable mitral closure is far more common in textbooks than real life.

To auscultate it is vital to ask the patient to lie on the left side and to use the bell. There is a mid-diastolic murmur which sounds like a drum beat and which is later in timing than a third sound and easy to miss. If you suspect the diagnosis but cannot hear anything abnormal, ask the patient to perform sit ups and then listen again. The more severe the mitral stenosis, the higher the left atrial pressure and the earlier will the left atrial pressure exceed the left ventricular pressure allowing the mitral valve to open. Severe mitral stenosis is therefore indicated by a murmur beginning soon after aortic closure and lasting until the end of diastole. However, it is vital to listen to a long cycle since in fast atrial fibrillation the murmur of even mild mitral stenosis may fill diastole.

In severe mitral stenosis there will also be wide splitting of the second sound. This is caused by delay of pulmonary closure as a result of pulmonary hypertension. The sign is the same as for mitral regurgitation but the mechanism is different. In patients still in sinus rhythm there will be presystolic accentuation of the murmur. If the mitral valve is still mobile there will be an opening snap. This sounds at best like a tiny hammer blow but more usually like a more than usually discrete start to the murmur.

Assessment

Echocardiography confirms the rheumatic aetiology with thickening of the tips of the leaflets extending down the chordae and the presence of commissural fusion (*Figure 9*). The stenosis is graded by a combination of planimetry of the orifice, and measures calculated from the continuous wave signal recorded across the valve (*Table 2*). The pressure half-time is a measure of depressurization of the left atrium. A long pressure half-time implies that blood takes a long time to enter the left ventricle and the mitral stenosis must be severe. The pressure half-time can be used to calculate a haemodynamic orifice area using the empirical Hatle formula: orifice area = 220/pressure half-time. Planimetered (or geometric) orifice area and haemodynamic orifice area are often similar but there may be discrepancies as a result of coexistent mitral or aortic regurgitation or left ventricular dysfunction. Mean gradient is calculated by the machine's software. Cardiac catheterization is a potentially inaccurate method of assessing mitral stenosis since there is a delay between left atrial and pulmonary wedge pressure trace leading to overestimation of the degree of stenosis.

The suitability for balloon valvotomy is judged from the appearance of the valve and chordae

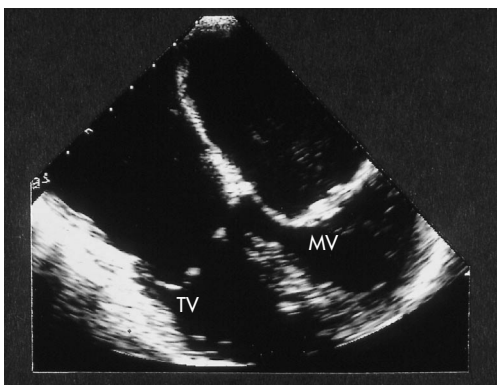

Figure 9. Rheumatic disease of the mitral and tricuspid valves on transoesophageal echocardiography. Both the mitral valve (MV) and tricuspid valve (TV) have thickened tips. However, as in this illustration, thickening is always more severe on the mitral than the tricuspid valve. Commissural fusion prevents excursion of the tips, but the main bodies of the valves are unthickened and mobile. Both valves therefore dome in diastole.

TABLE 2.
Guidelines to grading mitral regurgitation

	Mild	Moderate	Severe
Jet area (cm^2)	< 4.0	4.0–8.0	> 8.0
Jet width (cm)	< 0.4	0.4–0.6	> 0.6
Flow acceleration in left ventricle (cm^2)	< 0.3	0.3–0.5	> 0.5
Pulmonary vein flow	Normal	Blunted systolic	Systolic reversal
Continous wave signal	Low intensity	Less dense than forward flow	As dense as forward flow

(Wilkins et al, 1988). Valvotomy is contraindicated if there is heavy thickening and especially matting of the chords, calcium at the commissures, thickening and immobility of the valve, more than mild mitral regurgitation or thrombus on transoesophageal echocardiography.

The assessment must also include estimation of the pulmonary artery pressure. From the modified Bernoulli formula the pressure difference across the tricuspid valve is $4 \times v^2$ where v is the peak velocity of the tricuspid regurgitant signal. To this must be added an estimate of right atrial pressure which can be obtained from the degree of contraction of the inferior vena cava during inspiration. This is usually >50% if the right atrial pressure is 5–10 mmHg, but the inferior vena cava will be engorged and non-contractile if the right atrial pressure is >20 mmHg (Schiller, 1990). Finally echocardiography must check for signs of involvement of the aortic and tricuspid valves and also assess right ventricular size and function.

CONCLUSION

In mitral disease there is a wide difference in outcome between asymptomatic and symptomatic patients with the same degree of valve disease. If there is doubt the patient should be exercised. In genuinely asymptomatic severe disease, surgery may be indicated for early signs of ventricular dysfunction, mild right ventricular dysfunction in severe mitral stenosis and left ventricular systolic dilatation in severe mitral regurgitation. HM

KEY POINTS

- Mitral regurgitation usually occurs secondary to left ventricular dysfunction.
- The most common primary valvar cause is mitral prolapse.
- The signs of severe regurgitation are: displaced apex, loud pansystolic murmur, third heart sound and wide splitting of the second heart sound.
- Chronic severe mitral regurgitation causes progressive left ventricular fibrosis: contractile failure is likely if systolic function appears at the lower limit of normal (ejection fraction < 60%, fractional shortening < 29%).
- Surgery is indicated by symptoms or left ventricular dilatation.
- The mortality for unoperated symptomatic severe mitral stenosis is high.
- The signs of severe stenosis are: short gap between the second heart sound and the start of the murmur, long diastolic murmur and widely split second heart sound.
- The left ventricle is protected but mitral stenosis causes a progressive rise in pulmonary artery pressure ultimately leading to right ventricular failure.
- Surgery is indicated for symptoms or a progressive rise in pulmonary artery pressure or early right ventricular dilatation.

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