

MITRAL STENOSIS

Epidemiology

Mitral stenosis (MS) is highly prevalent in developing countries because of its association with rheumatic fever (6/1000 children in India vs 0.5/1000 in developed countries), but is also seen in developed countries where patients are of increased age.^{1,2} In developed countries, the prevalence of MS detected by echocardiography is about 0.1—0.2%.³ Although the attack rate for rheumatic fever is roughly equal among genders, MS is 2 to 3 times more common in women.

Aetiology

Rheumatic fever is the main cause of MS although most patients with symptomatic advanced rheumatic heart disease do not have a history of acute rheumatic heart disease.⁴ The M protein antigen held in common between the heart and group A hemolytic Streptococcus results in an autoimmune attack of the heart in response to streptococcal infection. The rheumatic process leads to inflammation of endocardium, myocardium and pericardium, but the disease affects mainly the endocardium.¹ Persistent inflammatory valve damage results in gradual progression that is strongly associated with repeated episodes of rheumatic fever. In the western world symptoms of MS usually appear after 15 to 20 years following the rheumatic fever attack. **Degenerative** causes may be seen in up to 12.5% in developed countries.⁵ In 6-8% of patients with severe **mitral annular calcification**, who are often elderly or dialysis-dependent, calcium encroaching into the valve leaflets causes mitral stenosis. Other rare causes are **congenital MS (Lutembacher syndrome when combined with ASD)**, **mucopolysaccharidoses**, **Fabry disease**, **systemic lupus erythematosus**, **rheumatoid arthritis**, **anorectic drugs**, and disorders associated with abnormal serotonin metabolism (**carcinoid and methysergide treatment**).¹

Pathophysiology and Natural History

The main features are leaflet thickening and calcification with chordal shortening and fusion. Patients usually have a dilated and stiff LA, and may develop systolic and diastolic LV dysfunction. Procoagulation abnormalities are common. The normal mitral valve area is 4-5 cm² and a gradient is rare unless the valve is less than 2 cm². The valve area narrows gradually by 0.1-0.3 cm² per year and symptoms start when mitral valve area becomes < 1.5 cm². Pulmonary oedema may develop with valve areas < 1 cm² (Table 1). Patients with pulmonary oedema rarely have severe pulmonary arterial hypertension, whereas those with

severe pulmonary hypertension (pulmonary vascular resistance $>6-8$ Wood units) seem to present with right heart failure rather than pulmonary oedema. The 10-year survival of untreated patients presenting with MS is 50% to 60%, depending on symptoms at presentation. Death in neglected cases is mainly due to heart failure or systemic embolism.^{2, 4} A transmitral gradient ≥ 8 mm Hg and right ventricular systolic pressure ≥ 50 mm Hg are more predictive of mortality than symptom status or comorbid conditions.⁶

Presentation

Patients usually present with **SOBOE** or **fatigue**.^{2, 4} Later symptoms include **haemoptysis** (pulmonary oedema or bronchial vein rupture), **chest pain**, and **systemic embolism**. The enlarged left atrium may impinge on the left recurrent laryngeal nerve, causing hoarseness (**Ortner's syndrome**). **Atrial fibrillation** occurs in approximately 50% of patients with mitral stenosis, precipitates such symptoms, greatly increases the risk of systemic embolization, and reduces cardiac output and exercise capacity. **Pulmonary arterial hypertension** is reversible, and resolves after intervention. Moderate-to-severe **tricuspid regurgitation** is seen in up to a third of patients with mitral stenosis and may not be improved with valvuloplasty, and if severe requires ring annuloplasty at time of mitral surgery. It usually results from RV dilation, and if severe requires ring annuloplasty at time of mitral surgery. **Rheumatic AR** is associated with MS that may blunt the presentation of AR due to reduced cardiac output.

Physical Examination

Mitral facies with plethoric bluish cheeks with telangiectases are now rarely seen.

A diastolic thrill may be palpated in the left lateral decubitus position.

Increased intensity of the S₁ because the transmitral gradient holds the mitral valve open for all of diastole, so that ventricular systole closes the mitral valve from a long moment arm. In advanced disease, S₁ may become soft.

Mitral valve opening snap. The distance from S₂ is a measure of MS severity. An S₂-opening snap interval <0.08 seconds usually indicates severe disease.

A low-pitched mitral rumble follows the opening snap. **Presystolic accentuation** of the murmur audible in normal sinus rhythm or during long RR intervals in atrial fibrillation indicates tight stenosis.

A high-pitched blowing murmur (**Graham Steell**) may be heard at the cardiac base. Although this murmur is thought to represent the PR of pulmonary hypertension, in reality it is more often due to concomitant AR.⁷

Pulse pressure may also be reduced in advanced disease.

Elevated JVP, TR, hepatomegaly, ascites, and peripheral edema may be found in severe pulmonary hypertension and RV failure.

P₂ increased in pulmonary hypertension.

Investigations

ECG Left-atrial enlargement (P wave > 0.12 sec in lead II or a deep negative P in V1) and RV hypertrophy, often with AF.

Chest radiography Left-atrial enlargement and in long-standing MS pulmonary congestion and pulmonary arterial hypertension. Interstitial oedema is manifested as Kerley A lines (dense, short, horizontal lines at the costophrenic angles) or Kerley B lines (straight, dense lines towards the hilum).

Echocardiography is used to exclude conditions that mimic mitral stenosis (atrial myxoma, tricuspid stenosis, ball-valve thrombus or ASD), calculate valve area diagnose, assess mitral regurgitation, and provide information about suitability for percutaneous balloon valvuloplasty (PBV).

Stenosis severity is determined by:

- **Planimetry.** The most reliable method to calculate valve area is planimetry with 2D or 3D echocardiography cross-section imaging. 2D echocardiography underestimates the severity of mitral stenosis, especially moderate-to-severe disease, and underestimates the extent of commissural splitting by PBV.
- Doppler-derived **pressure half-time.** Valve area is given by the empirical formula $220/\text{PHT}$ (Figures 1 and 2). This method is affected by left-ventricular chamber compliance, and heart rate.

Mitral stenosis severity should be carefully assessed in the setting of severe aortic stenosis, since it can be overestimated. Mitral valve area $\leq 1.5 \text{ cm}^2$, mitral annulus diameter $\leq 1 \text{ mm}$ or extension of calcification to both anterior and posterior mitral leaflets suggest the presence of true MS.⁸

Transoesophageal echocardiography provides an improved image of the commissural anatomy and calcification, and allows detection of left-atrial appendage thrombus and calculation of the echo score (Tables 2 and 3, and Figure 3).

Exercise or dobutamine stress echocardiography is needed for patients with inconclusive symptoms or haemodynamics.

Cardiac catheterisation is rarely needed with imaging methods there are now available (echo, cardiac CT, and CMR). It may be indicated when the noninvasive tests are inconclusive. Cardiac output and transvalvular gradient measurements are used to calculate valve area with the Gorlin formula and reassess stenosis severity (Figure 4). It may also be

used to assess the response of PA and LA pressures to exercise or to assess the cause of pulmonary arterial hypertension when it is disproportional to MS severity.

Coronary angiography is indicated only in patients with evidence of myocardial ischemia .

Therapy

Medical Therapy

Diuretics and β blockers or rate-affecting calcium channel blockers (eg, diltiazem) are the mainstay for control of heart rate. The role of statins in slowing progression of MS is under investigation.

Anticoagulation is indicated in AF, or prior embolic event or left atrial thrombus (Table 4).

A vitamin K antagonist rather than direct oral anticoagulants is preferred. Systemic embolization may occur in 10-20% of patients with MS even in the absence of left atrial thrombi. Retrospective studies indicate a 4-15-fold decrease in the incidence of embolic events with anticoagulation.

AF develops in 30-40% of patients and is associated with a poorer prognosis (10-year survival 25% compared to 46% in SR). Pharmaceutical or electrical cardioversion is recommended after transesophageal exclusion of left atrial thrombi or following 3 weeks of warfarin under IV heparin. Warfarin is continued after cardioversion for at least one month or indefinitely if indicated.

Interventional/Surgical Therapy

As with all valvular heart diseases, no randomized trials have been performed to ascertain the best timing of intervention. Recommendations are based on observational data.^{9, 10}

Percutaneous balloon valvuloplasty (PBV) improves survival especially in patients with NYHA class III or IV (Tables 5-7, and Figures 5,6). The technique is as effective as open valvotomy and more effective than closed valvotomy.¹¹ Nearly half of all patients who undergo percutaneous mitral commissurotomy remain free from cardiovascular death or surgery at 20 years, and 25% of them need a repeat procedure.¹² Successful BMV is usually defined as a post procedure mitral valve area of $>1.5 \text{ cm}^2$ with no more than moderate mitral regurgitation. Suitability for BVM is determined by valve morphology and the amount of mitral regurgitation present. The Wilkins score (Table 2) is the most widely used echo score and gives a rough guide to the suitability of the valve morphology for BMV. This scoring system assigns a point value from 1 to 4 for each of (1) valve calcification, (2) leaflet mobility, (3) leaflet thickening, and (4) disease of the subvalvular apparatus. In general, patients with a score of <8 -9, no calcification and less than moderate mitral regurgitation, have the best outcomes, although many patients have benefited from BMV despite higher valve scores. A novel scoring system incorporating new quantitative echocardiographic

parameters is more accurate in predicting outcome following PMBV (Table 2).¹³ According to this scoring system, three risk groups were defined: low (score of 0–3), intermediate (score of 5), and high (score of 6–11) with observed suboptimal PMBV results of 16.9%, 56.3%, and 73.8%, respectively. Severe valve calcification, especially when it is unilateral, is not necessarily a contraindication for the procedure.^{14 15} Patients with favourable morphology have more than 90% procedural success, and a benefit of PBV has been demonstrated in asymptomatic patients with moderate MS (<1.5 m²) and suitable morphology, even in the absence of other conventional indication for intervention.¹⁶ Procedural mortality is nowadays <1%, and is mainly due to tamponade or severe mitral regurgitation. Complications include severe mitral regurgitation (2-10% although 25% of patients increase severity by one grade) most often due to non-commissural tear, urgent surgery (<1%), haemopericardium (0.5-12%), embolism (0.5-5%), and residual ASD (<5%). Re-stenosis can often be treated with repeat PBV but results are poorer than are those after the first intervention. Of patients with a good result, 10% will require re-PBV, and 30% surgery in the next 20 years.¹² In asymptomatic patients severe MS, early PBV did not significantly reduce the incidence of cardiovascular events among with during a median follow-up of 6 years.¹⁶ Recommendations for the management of AF are provided in the relevant Chapter.

Open valvotomy is attractive in cases unsuitable for PBV and allows conservation of the native valve, controlled reconstruction of the valves, and simultaneous tricuspid valve repair or mitral valve replacement if necessary. The risk of surgery is 1-3%.¹ Patients with mitral stenosis and severe tricuspid regurgitation do better with surgical repair than with PBV.

Mitral valve replacement with preservation of the subvalvar apparatus is the treatment of choice in elderly patients with anatomy that is unfavourable for other options. Patient prosthesis mismatch and prosthesis stenosis due to in-growth of pannus are the main problems. The operative risk is <5% in the absence of other comorbidities but may reach 20% in the elderly with pulmonary hypertension.^{9, 17} The choice of a **mechanical or bioprosthetic** valve is discussed in detail in the Chapter on Prosthetic Valves.

Congenital MS is rare. The typical echocardiography appearance is of parachute-like mitral stenosis with a circular orifice and no commissures.¹⁸ Surgery is indicated with a mean MV gradient >10 mm Hg in the presence of symptoms or a PA pressure >50 mm Hg.

Concomitant surgical ablation with a modification of the MAZE or alternative procedures may be needed in the case of drug-refractory AF.¹⁹

Transcatheter mitral valve replacement utilizing aortic balloon-expandable transcatheter heart valves has been used to treat patients with failed surgical bioprostheses, failed repairs with surgical rings, or severe mitral annular calcification who are not candidates for surgery.²⁰ In a STS Registry on mainly the SAPIEN S3U valve, results were excellent for degenerated prosthetic valves in low/intermediate risk patients.²¹

Non-cardiac surgery

In asymptomatic patients with significant MS and a systolic pulmonary artery pressure <50 mmHg, non-cardiac surgery can be performed safely. In symptomatic patients or in patients with systolic pulmonary artery pressure >50 mmHg, percutaneous mitral commissurotomy should be attempted before non-cardiac surgery if it is intermediate- or high-risk. If valve replacement is needed, the decision should be individualized. If valve morphology is not favorable for percutaneous commissurotomy, moderate-risk elective noncardiac surgery can be performed in asymptomatic, severe MS with appropriate intraoperative and postoperative hemodynamic monitoring. Recommendations are provided in Table 8.

Exercise

Recommendations for exercise and participation in sports are provided in Table 9.

Pregnancy

Mitral stenosis in pregnancy is associated with substantial morbidity (including pulmonary oedema), even in asymptomatic or minimally symptomatic patients with mild-to-moderate disease (mitral valve area $1-1.5 \text{ cm}^2$). In the international Registry of Pregnancy and Cardiac Disease, although mortality was only 1.9% during pregnancy, $\approx 50\%$ of the patients with severe rheumatic MS and 23% of those with significant MR developed heart failure during pregnancy. Thus, percutaneous balloon mitral commissurotomy may be a feasible treatment for young women with moderate or severe mitral stenosis who have a desire for pregnancy, even if they are asymptomatic.²²

References

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