MITRAL STENOSIS

Most common cause of Mitral stenosis [MS] is rheumatic heart disease [RHD]. Approximately 25% of all patients with rheumatic heart disease have pure MS, and an additional 40% have combined MS and mitral regurgitation [MR] [1-3]. Two thirds of all patients with MS are female. Pathological process by which rheumatic fever causes MS includes leaflet thickening and calcification, commissural fusion, chordal fusion, or a combination of these processes [4, 5].

Normal mitral valve [MV] area is 4.0 - 6.0 cm². When the orifice is reduced to < 2 cm², blood flow occurs from left atrium [LA] to left ventricle [LV] only if propelled by a pressure gradient. This results in elevation of left atrial pressure, which is reflected back into the pulmonary venous circulation thereby increasing pulmonary venous pressure [PVH]. This ultimately leads to pulmonary arterial hypertension [PAH], right ventricular [RV] dysfunction and tricuspid regurgitation [TR].

Definite symptoms typically occur only with a substantial reduction in mitral valve orifice area [MVOA] usually to < 1.0 cm². However, functional limitation occurs gradually and many patients experience exercise limitation at a larger valve area (1 to 2 cm²).

Symptoms: Most common presenting symptoms of MS are progressive exertional dyspnea and fatigue which may be accompanied by cough and wheezing. Orthopnea and paroxysmal nocturnal dyspnea [PND] occur as the disease progresses. Episodes of acute pulmonary edema may be precipitated by effort, emotional stress, infection, atrial fibrillation [AF] with fast ventricular rate [FVR] or pregnancy. Symptoms of right heart failure may supervene when pulmonary vascular resistance increases markedly.

Hemoptysis is rare. But it can be sudden and severe, due to rupture of thin walled, dilated bronchial veins. Milder degrees of hemoptysis may be caused by pulmonary infarction and winter bronchitis. It may be also seen during episodes of PND and pulmonary edema.

Chest pain typical of angina is seen in 15% of patients with MS which may be caused by RV hypertension. Atrial fibrillation is the most common complication of MS and systemic embolism occurs in 20% of patients. Infective endocarditis is rare. Compression of the left recurrent laryngeal nerve by dilated left atrium, pulmonary artery or enlarged tracheobronchial lymph nodes may cause hoarseness of voice [Ortner syndrome].

Physical signs: Arterial pulse is usually normal but in patients with a reduced stroke volume pulse may be low in volume. Pulse is irregular in patients with AF and opening snap [OS] suggest pliable anterior mitral leaflet [AML]. RV lift and a loud palpable P2 are common in patients with PH. Low pitched rumbling diastolic murmur, best heard at the apex is the hallmark of MS. Long diastolic murmur with presystolic accentuation and a short A2 –OS interval suggest tight MS. Loud S1 and OS indicate leaflet pliability and do not predict severity.

Murmur of MS may be soft or inaudible in patients with very severe MS, severe PH, congestive cardiac failure [CCF], extensive calcification and subvalvar disease and marked RV enlargement. Intensity may also be reduced in associated diseases like aortic stenosis [AS], aortic regurgitation [AR] and atrial septal defect [ASD]. Obesity, thick chest wall and COPD can also attenuate the murmur of MS.

ECG: Left atrial [LA] enlargement is the earliest finding seen in 90% of patients with significant MS. Atrial fibrillation occurs in 30 – 40% and the incidence increases with increasing age. RVH, right axis deviation and right atrial enlargement [RAE] are seen in patients with PAH and TR.

Chest X Ray findings of MS are summarised in Table 1

ECG findings: Echocardiography plays a central role in the diagnosis and management of MS [fig 1]. Findings are summarized in Table 2
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Table 2: Echo findings in MS

1. Thickening of leaflets and subvalvular apparatus
2. Restricted movement of the mitral leaflets
3. Fusion of commissures
4. Diastolic doming of AML
5. MVOA decreases – fish mouth appearance
6. Turbulent high velocity flow with increased gradient
7. LAE, RVH, PH, TR
8. LA Thrombus (Figure 2)

Fig. 1: ECHO – MS

Fig. 2: LA CLOT

open mitral valvotomy [OMV] / Mitral valve replacement [MVR]

Medical Therapy:
1. Medical management of MS is primarily directed toward
2. Prevention of recurrent rheumatic fever with penicillin prophylaxis as per established guidelines
4. Monitoring disease progression to allow intervention at the optimal time point.

In general, all patients with MS should undergo antibiotic prophylaxis against infective endocarditis for those procedures known to cause bacteremia. Diuretics are useful for treating mild symptoms. B blockers attenuate the increases in heart rate especially during exertion and optimise diastolic filling. Digoxin has no role in patients with MS and sinus rhythm. Anemia and infections should be treated promptly and aggressively.

AF commonly accompanies MS and is more related to age than to stenosis severity. When AF occurs acutely, it is often associated with a rapid ventricular response. As increased heart rate primarily reduces time in diastole, it causes further impairment in left ventricular filling, which leads to abrupt left atrial hypertension and reduced cardiac output. Immediate rate control is imperative and can be done by administration of B blockers or rate-reducing calcium channel blockers [diltiazem & verapamil]. If these therapies are ineffective in controlling rate and the patient is unstable, immediate DC cardioversion is indicated.

Patients with MS in chronic AF are at risk of embolic stroke (at a rate of 7% - 15% per year) [14]. Accordingly, all such patients require warfarin anticoagulation with a target international normalized ratio of 2.0 to 3.0. After a first embolic event, the recurrence rate is increased 2-fold without anticoagulation.

Chronic rate control is achieved with digoxin, B blocker, a calcium channel blocker, or some combination of these agents. Adequacy
of rate control should be monitored not only at rest but also during activity, because in many patients, apparently adequate rate control at rest belies tachycardia with even mild activity. Such patients are at risk for developing tachycardia-induced cardiomyopathy.

### BALLOON VALVOTOMY

In the last two decades, BMV has become the treatment of choice for patients with symptomatic rheumatic MS. Since its introduction in 1984 by Inoue et al. [15], BMV by Inoue technique has been widely used in the treatment of mitral stenosis. Several studies have reported good immediate, short-term and long-term results [16–24].

Given the excellent hemodynamic and functional results of percutaneous mitral commissurotomy, especially when the valve leaflets are thin and mobile, it is reasonable to consider intervention earlier in the disease course both to prevent atrial fibrillation and pulmonary hypertension and to preserve functional status, particularly in young individuals. Patient selection is based on clinical evaluation and echocardiographic assessment of disease severity [Table 3] and valve morphology.

### INDICATIONS FOR BMV:

BMV is indicated in patients with moderate to severe MS in the absence of LA thrombus and not more than mild MR:

1. Symptomatic (NYHA functional class II, - IV) with valve morphology favorable for PTMC
2. Asymptomatic patients who have pulmonary hypertension [pulmonary artery systolic pressure > 50 mm Hg at rest or > 60 mm Hg with exercise]
3. Symptomatic patients who are either not candidates for surgery or are at high risk for surgery.

### Table 3: Assessment of severity of MS

<table>
<thead>
<tr>
<th>Severity</th>
<th>Mean gradient</th>
<th>MVOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>NORMAL</td>
<td>---</td>
<td>4 – 6cm²</td>
</tr>
<tr>
<td>MILD MS</td>
<td>&lt; 5mmHg</td>
<td>1.5 - 2cm²</td>
</tr>
<tr>
<td>MODERATE MS</td>
<td>5 – 10mmHg</td>
<td>1.0 – 1.5cm²</td>
</tr>
<tr>
<td>SEVERE MS</td>
<td>&gt; 10 mmHg</td>
<td>&lt; 1.0cm²</td>
</tr>
</tbody>
</table>

### Table 4: Expanding indications for PTMC

1. Mitral Restenosis
2. Mitral Stenosis with LA Clot [type Ia, Ib & Iia]
3. Moderate Mitral Regurgitation (Central Jets)
4. Hybrid Therapy - AR, AS, CABG
5. Lutembacher’s syndrome

### Table 5: Contraindications for PTMC

1. Left atrial body clot
2. Grade 2 or more MR
3. Bicommissural calcification
4. Lack of expertise

BMV is also considered in the following subset of patients [Table 4]:

PTMC is contraindicated in following situations [Table 5]:

**Technique:** Transseptal technique is the most common technique used to perform BMV. Self positioning Accura or Inoue balloon is advanced over the wire across the interatrial septum after transseptal puncture. Ballon is inflated after positioning it across the mitral valve [fig 2]. Stepwise dilatation with gradual increase of balloon size is performed which is guided by the echocardiographic and hemodynamic assessment.

BMV is considered to be successful if post procedural MVOA > 1.5cm² or if there is 50% increase in MVOA compared to pre procedure valve area and MR not more than mild with adequate split of one of the commissure [fig 3].

**Immediate hemodynamic results:**

MVOA increases from an average of 1cm² to 2cm². Transmirtal pressure gradient reduces from an average of 18 to 6 mm Hg.
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Among 12,555 patients who underwent BMV in our hospital, 605 were pregnant. Majority were in NYHA class III and IV. 47 out of 12,555 patients who underwent BMV in our hospital, before 20 weeks of pregnancy, using single balloon [Inoue or Acura] is reduced by abdominal & pelvic shielding, avoiding the procedure 0.5 rad, far below the established limit of 5 rads. Risk of radiation in the third trimester during which radiation risk to the fetus is negligible. Optimal timing of BMV is end of 2nd trimester or beginning of labor and delivery. Compared to surgical commissurotomy, BMV has been excellent, with few maternal or fetal complications [25].

Without intervention maternal mortality is significantly higher [6.8%] for those in NYHA classes III and IV, particularly during labor and delivery. Compared to surgical commissurotomy, BMV has been shown to yield similar immediate and long term results with lower maternal and fetal mortality.

Now we have more than 15 year experience of BMV either with very limited fluoroscopy [2-5 minutes of exposure] or echocardiographic guidance. The reported results of BMV have been excellent, with few maternal or fetal complications [25]. Optimal timing of BMV is end of 2nd trimester or beginning of third trimester during which radiation risk to the fetus is negligible. During BMV average amount of radiation received by the fetus is 0.5 rad, far below the established limit of 5 rads. Risk of radiation is reduced by abdominal & pelvic shielding, avoiding the procedure before 20 weeks of pregnancy using single balloon [Inoue or Acura] rather than double balloon and minimizing fluoroscopy time [26].

Out of 12,555 patients who underwent BMV in our hospital, 605 were pregnant. Majority were in NYHA class III and IV. 47 patients were in acute pulmonary edema. Single balloon [Inoue or Acura] was used in all the patients. Average fluoroscopy time was 5.1±2.5 mins. Procedure was successful in 95.2% of patients. Mean left atrial pressure dropped from 32±16 to 14±5 mm Hg and mitral valve orifice area increased from 0.8±0.4 to 1.85±0.03 cm². Mild to moderate MR was seen in 10.5% of patients and 1.6% had severe MR. Serious complications like tamponade occurred in 1.8%, CVA in 0.4% and mortality in 0.7% of patients.

**BMV in patients with Left Atrial Thrombus:**

LA thrombus occurs in 3–13% of patients with MS and its presence is generally considered as a contraindication for BMV [27]. Systemic embolization occurs in 0.3–0.8% of patients during or shortly after the procedure and represents a potentially devastating complication.

Our center has performed more than 12,000 BMVs in the last 15 years. On many occasions we were compelled to perform BMV in the presence of LA/LA appendage thrombus as a bail out procedure in emergency situations. In all these situations, to minimize the risk of embolic complications, we adopted a modification of the wire technique described earlier [28]. Encouraged by this we conducted a prospective study of BMV in 108 patients with LA thrombus between January 2005 and December 2007[29].

We classified LA thrombus based on their location, extension, and mobility as assessed by TTE/TEE as follows: [Fig 5]

**Type Ia:** LA appendage clot confined to appendage.

**Type Ib:** LA appendage clot protruding into LA cavity.

**Type Ia:** LA roof clot limited to a plane above the plane of fossa ovalis.

**Type Ib:** LA roof clot extending below the plane of fossa ovalis.

**Type IIa:** Layered clot over the interatrial septum (IAS).

**Type IIb:** Mobile clot which is attached to LA free wall or roof or IAS.

**Type III:** LA appendage clot confined to appendage.

**Type IV:** Ball valve thrombus (Free Floating).

Patients were included in the study if they had type Ia (n - 69), type Ib (n -35) and type IIa (n - 4) LA clots. All these patients were adequately anticoagulated (INR 2.0–3.0) for 8–12 weeks.

All patients underwent BMV by modified over the wire technique. There was significant and comparable improvement in the mitral valve area, mitral valve gradient, LA mean and pulmonary artery systolic pressure following the procedure. There were no thromboembolic episodes during the procedure. However, there was one case of transient ischemic attack which occurred 6 hr after a successful BMV.

Hence in selected patients of mitral stenosis with LA thrombus (type Ia, Ib, and IIa), BMV can be performed safely with the modified
over the wire technique. Systemic thromboembolism, technical failures and other complications are very rare when performed by experienced operators.

**BMV in juvenile MS**

Special features of Mitral Stenosis in children are fibrotic, rubbery valve with severe sub-valvular disease. Calcification is rare and atrial fibrillation is less common. Significant pulmonary arterial hypertension is seen in majority of children.

In our series of 12,550 cases, 4% were less than 10 years [youngest was 7 year old] and 14% were in the age range of 10–20 years. BMV in children appears to be safe and effective similar to adult patients. In the long term follow up there was no significant difference in the incidence of restenosis and event free survival.

**BMV in patients with moderate MR**

BMV may be successful in a small subset of patients with moderate MR when the jet is central with minimal non coaptation of the leaflets and noncalcified commissures.

**BMV in Mitral restenosis**

Definition of mitral restenosis is return of symptoms with > 50% loss of post valvotomy MVOA or MVOA at follow up < 1.5cm². Restenosis rate for BMV is 5 - 8% Over 8 Years [OMV - 7 to 11%, CMV - 10 - 20%].

BMV is safe and provides good immediate results in patients with restenosis. Long term results are satisfactory [though inferior to de novo MS] with more than half of the patients remaining minimally symptomatic at 10 years enabling the reoperation to be deferred.

**BMV in Lutembacher's Syndrome:**

Ideal strategy is surgical closure of ASD with OMV/MVR. But in critically ill patients surgery carries a higher risk. In such patients BMV restores hemodynamics and improves metabolic parameters. After a few weeks ASD closure can be done electively.

**Hybrid Therapy – BMV in patients with AR,AS**

In patients with combined MS and significant aortic valve disease balloon mitral valvotomy followed by AVR may be performed [27]. This obviates the need for double-valve replacement, which has a higher risk of perioperative mortality and postoperative complications than single-valve replacement (30). In most cases, it is advisable to perform balloon mitral valvotomy first and then monitor the patient for symptomatic improvement. If symptoms disappear, AVR can be delayed.

**Indications for mitral valve surgery in patients with MS:** [closed/open mitral valvotomy or mitral valve replacement]

Symptomatic patients with moderate or severe MS when

1. PTMC is not available [closed mitral valvotomy]

2. PTMC is contraindicated [Table 5] because of left atrial thrombus despite anticoagulation [OMV if valve morphology is suitable] or because of concomitant moderate to severe MR [MVR]

3. Mitral valve morphology is not favorable for PTMC, in a patient with acceptable operative risk [MVR].

**MITRAL REGURGITATION**

Proper functioning of the mitral valvular complex depends on the structural and functional integrity of its individual components - mitral annulus, leaflets, chordae tendinae, papillary muscles, left atrial and left ventricular walls in continuity with the leaflets, and papillary muscles. MR can be classified as primary, due to abnormality of the mitral valve apparatus (e.g., rheumatic or degenerative mitral valve disease), or secondary (or functional), as a result of an ischemic or nonischemic dilated cardiomyopathy in the setting of anatomically normal mitral valvular leaflets and chords.

Despite the superior long-term outcomes associated with mitral valve repair rather than mitral valve replacement, mitral valve repair is performed in only one-third of patients undergoing mitral valve surgery.

**Annuloplasty** is the cornerstone of mitral valve repair and is essential for the surgical correction of functional MR. For repair of degenerative mitral valve disease: failure to perform a concomitant annuloplasty procedure adversely affects the long term durability of the repair. Annuloplasty may be used concomitantly with leaflet repair (resection, sliding annuloplasty) or chordal reconstruction (transposition, artificial chords). The Alfieri procedure involves suturing the free edges of the middle anterior (A2) and posterior (P2) leaflets of the mitral valve. This produces a **double orifice mitral valve**. This procedure can be used to treat degenerative or functional MR. Same principle is used in **transcatheter edge-to-edge repair technique** [31].

**Strategies for transcatheter mitral valve repair:**

1. Creation of a **double orifice mitral valve** using percutaneous edge-to-edge techniques with a clip device [Mitra-Clip] or stitch [Mobius]

2. **Remodeling of the annulus** of the mitral valve by suture-based techniques (e.g., Percutaneous Suture Annuloplasty), or application of radiofrequency energy

3. **Remodeling of the mitral valvar complex** by transventricular (e.g., iCoapsys) or transatrial (e.g., Percutaneous Septal Sinus shortening) devices.

4. Remodeling of the annulus of the mitral valve by devices implanted in the coronary sinus (e.g., Percutaneous Mitral Annuloplasty device).

A number of transcatheter mitral valve therapies are currently under various phases of clinical trials.
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Fig. 6: Mitra clip and double orifice MV with Mitra clip

**Edge-to-Edge Technique - MitraClip:** The MitraClip uses a tri-axial catheter system with a clip device at its distal tip (Fig. 6). The goal of the procedure is to create a double orifice mitral valve similar to the Alfieri surgical technique. The guide catheter is 24-F at its proximal end, tapering to 22-F at its distal end. The system is delivered via a standard transseptal approach into the left atrium. The 2-armed clip is a polyester-covered device. Each clip arm opposes against a multipronged friction element that allows up to 8 mm of mitral valve leaflet to be grasped securely on each side. Once clip placement and real-time echocardiography confirm adequate reduction of MR (grade < 2+), the clip device is detached from the delivery catheter. Use of standardized echocardiographic protocols can greatly improve procedural times and ease of clip placement. The EVEREST (Endovascular Valve Edge-to-Edge Repair Study) phase I clinical study is completed and EVEREST phase II is currently enrolling patients with degenerative or functional MR.

**Conclusion:** BMV is the procedure of choice in the treatment of rheumatic mitral stenosis with excellent immediate and long term results. It is safe and effective across wide spectrum of clinical subset of patients with MS. Echocardiography before and during the procedure optimizes the outcome. Over the wire technique is useful in difficult entry situations & in patients with LA thrombus (Type la, lb & Ila).

A number of transcatheter mitral valve therapies for MR are currently evolving. It may obviate the need for surgeries in future.

**REFERENCES:**


