Current Evaluation and Management of Patients With Mitral Stenosis

Shahbudin H. Rahimtoola, MB, FRCP; Alex Durairaj, MD; Anil Mehra, MD; Ismael Nuno, MD

Case presentation: A 28-year-old woman with known mitral stenosis (MS) who was not taking antibiotic prophylaxis presented with new onset of chest pain, atrial fibrillation, and “heart failure.” She was treated for “heart failure” and converted spontaneously to sinus rhythm. Echocardiographic/Doppler studies showed a mitral valve gradient (MVG) of 7, a mitral valve area (MVA) of 1.2 cm², 2+ mitral regurgitation (MR), no tricuspid regurgitation, normal left ventricular (LV) size and function, no left atrium (LA) thrombus, and a mitral valve score (University of Southern California [USC] scoring system) of 1, with no calcium in the commissures. At cardiac catheterization, mean pulmonary artery (PA) wedge was 23 mm Hg, mean PA pressure was 25 mm Hg, MVG was 10 mm Hg, and MVA was 1.2 cm². On exercise, mean PA wedge was 30 mm Hg, mean PA pressure was 55 mm Hg, and MVG was 18 mm Hg. On angiography, the LV end-diastolic volume was 80 mL/m², ejection fraction was 0.48, and 2+ MR, with normal coronary arteries. After catheter balloon commissurotomy (CBC), the MVA was 2.0 cm², mean PA wedge was 13 mm Hg, and mean PA pressure was 20 mm Hg, with no MR. Her discharge medications were penicillin V 250 mg twice daily and antibiotic prophylaxis for prevention of infective endocarditis.

Current Evaluations and Management of MS

Severity of MS

The relationship of the MVG as a function of the rate of mitral valve flow per diastolic second for various MVAs is shown in Figure 1. The threshold of onset of pulmonary edema is \( \approx 20 \text{ mm Hg} \). Assuming a normal mean LV diastolic pressure (LVDP) of 5 mm Hg, a mean MVG of 20 mm Hg would be necessary \(^1\) to maintain a normal cardiac output (CO). This is a level of LA pressure at which stage 2 of pulmonary edema (interstitial) would be present. An MVG of \( \approx 15 \text{ mm Hg} \) would be needed to reach stage 1 pulmonary edema (pulmonary congestion). If the LVDP were 10 mm Hg, stage 2 would be reached at a MVG of 15 mm Hg (Figure 1). The abnormalities that occur and the outcome of the patient depend on the MVA and LA pressure (Figure 2). The severity of MS can be graded on basis of the threshold of pulmonary edema at a certain cardiac output, heart rate, and MVA. The approximate values at a rate of 60 bpm are:

<table>
<thead>
<tr>
<th>Cardiac Output, L/min</th>
<th>MDF, mL/s</th>
<th>MVA, cm²</th>
<th>Severity of Mitral Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.0–12.0</td>
<td>300</td>
<td>&gt;2.0</td>
<td>Very mild</td>
</tr>
<tr>
<td>7.0–9.0</td>
<td>200</td>
<td>&gt;1.5 to 2.0</td>
<td>Mild</td>
</tr>
<tr>
<td>5.5–6.5</td>
<td>150–175</td>
<td>&gt;1.0 to 1.5(^*)</td>
<td>Moderate</td>
</tr>
<tr>
<td>4.5–5.0</td>
<td>125</td>
<td>1.0</td>
<td>Severe</td>
</tr>
</tbody>
</table>

\(^*\) In some patients with MVA \( \leq 1.1 \text{ cm}^2 \), the threshold of pulmonary edema is reached at a lower cardiac output. They have elevated mean PA wedge and mean PA pressures at rest and on exercise but not as high as in those with MVA \( \leq 1.0 \text{ cm}^2 \). These patients should be considered to have severe MS.\(^2\)

Evaluation of Patients With MS

A list of methods to diagnose MS and assess its severity and suitability for CBC, as well as to assess associated lesions, is depicted in Table 1; the important ones are highlighted. Clinical evaluation can accurately diagnose moderate or severe MS in 92% of patients.\(^3\)
A short A2-OS interval and long mitral diastolic murmur indicate severe MS. A good chest x-ray provides information about elevated LA pressures; pulmonary congestion occurs with an LA pressure ≥18 mm Hg, interstitial edema with an LA pressure ≥25 mm Hg, and alveolar edema with LA pressure ≥35 mm Hg. Signs of PA hypertension (loud P2, right ventricular hypertrophy) in absence of another cause indicate severe MS.

A comprehensive echocardiographic Doppler study is important. MVA by Doppler half-time, when MR/aortic regurgitation (AR) are absent or trivial, is reasonably reproducible. It is essential that mitral valve morphology using a scoring system [Massachusetts General Hospital [MGH] 1 to 16; USC 0 to 4],3 or the French,4 presence of LA thrombus, and assessment of MR and its severity are carefully evaluated. Transesophageal echocardiography is important if the patient is a candidate for CBC or surgical valve repair.

Cardiac catheterization and angiography are essential in many patients. If a comprehensive, high quality echocardiographic/Doppler study is evaluated by a skilled echocardiographer experienced in studying valvular heart disease, the findings are consistent with that of a careful and thorough clinical evaluation by a competent and skilled clinician in valvular heart diseases, and the patient is <35 years of age with no indications for coronary arteriography, then catheterization is not necessary in isolated MS.

Simultaneous LV and good quality PA wedge or LA pressures with measurement of CO yield MVAs that are reasonably reproducible. LV angiogram provides information about MR and allows calculation of LV volumes and ejection fraction; LV ejection fraction is below normal in approximately one third of patients with MS.1 In patients with valvular heart disease, assessment of associated coronary artery disease can only be provided by selective coronary arteriography.

Management of Patients With MS

Medical Therapy

Medical therapies are shown in Table 2. Patients with MS need antibiotic prophylaxis for prevention of recurrence of rheumatic fever and for prevention of infective endocarditis as recommended by the American Heart Association.5

Atrial fibrillation with a rapid ventricular rate impairs filling of the LV because of a reduction of diastolic filling time and loss of atrial contraction, which lead to decrease of CO and further increases of LA pressure. The patient is also at a risk for systemic emboli. Patients should be given anticoagulants and ventricular rate should be controlled.6 If the MS is severe, the patient should be converted to sinus rhythm after interventional therapy.

### Figure 2. Pathophysiology of MS

Important factors in determining outcomes are the severity of MS and severity of LA hypertension. RVH indicates right ventricular hypertrophy; RV, right ventricular; TR, tricuspid regurgitation; and RVE, right ventricular enlargement.

### Management of Patients With MS

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Interventional Therapy

Detailed management strategies are shown in Algorithms 1 to 5.

Follow-up times* in the algorithms are variable:

- They relate to when patient is seen by a cardiologist.
- Patient should be seen sooner by a cardiologist if there is any change in the patient’s condition.

### TABLE 1. Assessment of Patient With Mitral Stenosis

<table>
<thead>
<tr>
<th>Clinical History</th>
<th>Physical examination</th>
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<tbody>
<tr>
<td>Loud S$_1$</td>
<td>A$_2$—OS interval, length of MDM</td>
</tr>
<tr>
<td>Loud P$_2$, RVH</td>
<td></td>
</tr>
</tbody>
</table>

- Pulmonary edema (congestion, interstitial, alveolar)
- Enlargement of LA and other cardiac chambers

ECG

- Rhythm
- LA enlargement
- RV and LV hypertrophy

Echocardiogram/Doppler (BP at time of study must be recorded)

M-mode

- LV and LA dimensions absolute and corrected for BSA

2 Dimensional/Doppler

- MVA (Doppler half time, planimetry)
- Mitral valve morphology
  - Score
  - Ca++ in one or both commissures

- LA thrombus
- MR severity
- PA pressure
- Mean MVG
- LV volumes, measured LVEF
- Other valve lesions

Transesophageal echocardiography, if necessary

Treadmill test

- Assessment of exercise capacity, if necessary

Cardiac catheterization/angiography

- MVA
- Mean PA wedge/LA pressure
- PA pressures: systolic, diastolic, mean
- Mean MVG
- Cardiac output/cardiac index
- Pulmonary and systemic vascular resistances
- MR severity
- LV volumes and EF
- Right heart pressures
- Other valve lesions

Coronary arteriography

- Patients aged ≥35 years
- Patients aged <35 years
  - LV dysfunction
  - Symptoms or signs suggestive of CAD

Other or more risk factors for premature CAD (excluding sex)

- RVH indicates right ventricular hypertrophy; MDM, mitral diastolic murmur; BP, blood pressure; BSA, body surface area; EF, ejection fraction; and CAD, coronary artery disease.

### TABLE 2. Medical Treatment of Mitral Stenosis

| Antibiotic prophylaxis |
| Recurrent rheumatic fever |
| Infective endocarditis |

Restrict activities (moderate/severe MS)

- Severe exercise
- Competitive sports

Arrhythmias

- Prevent or control
  - Atrial fibrillation/flutter:
    - Control ventricular rate
    - Anticoagulation: start with IV heparin and warfarin: When INR is 2 to 3 discontinue heparin
    - Restore sinus rhythm

Cardiac medications

- Warfarin anticoagulation: INR at 2 to 3
  - Atrial fibrillation/supraventricular arrhythmias
  - Systemic emboli
  - LA thrombus
  - Pulmonary emboli
  - LV systolic dysfunction

Elevated pulmonary venous pressure: diuretics*

- "Heart failure"
  - Pulmonary congestion: diuretics*
  - Pulmonary edema: diuretics,* venodilators if necessary*
  - LV systolic dysfunction: digitals, ACE-inhibitors
  - Elevated systemic venous pressure and fluid retention: digitals, diuretics, ACE-inhibitors; β-blockers (second generation) after patients are stabilized and there is LV systolic dysfunction.

Follow-up (see Algorithms)

*Use judiciously; patients with severe MS need an elevated LA pressure to maintain adequate LV filling and CO.

### Algorithm 2.

**Interventional Therapy**

Detailed management strategies are shown in Algorithms 1 to 5. Follow-up times* in the algorithms are variable:

- They relate to when patient is seen by a cardiologist.
- Patient should be seen sooner by a cardiologist if there is any change in the patient’s condition.
When seen by a cardiologist, patient should have a history, physical examination, ECG, chest x-ray, and echocardiogram/Doppler. Additional tests should be performed, if necessary.

Patient should be seen at more frequent intervals by the primary care physician (family practitioner/internist/cardiologist) at which times only a history, physical examination, ECG, and chest x-ray should be performed.

**Catheter Balloon Commissurotomy**

CBC is the procedure of choice if indicated (Algorithms) and there are no contraindications (Table 3). In the United States, CBC is most commonly performed using the Inoue balloon (Toray Medical Co, Ltd). CBC is the procedure of choice because:

- Hospital mortality rate in the past 10 years has been close to zero.4,7
- The success rate is ≥95%.4
- The MVA increases to an average of 1.9 to 2.0 cm².4,5,7
- There are reductions of MVG, LA (PA wedge), and PA pressures, and an increase of CO; 60% of patients improve to New York Heart Association functional class (NYHA FC) I and 30% to NYHA FC II,4,7 which has been objectively documented by exercise tests.7
- A good immediate result is obtained in ≈89% of patients.4
- A closed mitral commissurotomy in a nonrandomized study in the 1950s and 1960s has shown an improved survival in symptomatic patients (NYHA FC II and III–IV) when compared with medical therapy.5

Surgical Valve Repair

If the valve is suitable for CBC but there are contraindications for CBC, surgical valve repair is the procedure of choice when appropriate skill and experience are available.

**MVR**

- MVAs after MVR and CBC are similar (Figure 4).
- Operative mortality rate is 2% to 7%.5,8,9
- Prosthesis-related mortality averages 2.5% per year (range: 2% to 3% per year), and prosthesis-related complications average 5% per year (range: 2% to 6% per year).5,8
- Use of a mechanical valve necessitates use of anticoagulant therapy with its resultant problems and complications.
- The insertion of a bioprosthesis to avoid anticoagulation-related problems and complications is associated with structural valve deterioration. In young people (16 to 40 years of age), structural valve deterioration begins at 2 to 3 years and is ≥60% at 10 years. Even in people aged 41 to 60 years, bioprosthesis is associated with high structural valve deterioration up to 50%, and 50% of the late mortality is a consequence of structural valve deterioration.

**MVR Versus CBC**

MVR is usually recommended in patients who are in NYHA FC III and IV (Algorithm) because of the above listed increased mortality and morbidity associated with MVR. MVR should also be considered in patients who are in NYHA FC II and have moderate or severe pulmonary hypertension, and in those who are in NYHA FC I (asymptomatic) if they

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**TABLE 3. Contraindications (Absolute/Relative to CBC for MS)**

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**Algorithm 3.**

- In randomized trials, the results of CBC versus closed surgical commissurotomy or surgical repair by open procedures are similar.5
- Follow-up to 10 years after CBC shows very good event-free survival (Figure 3A).4 There were no deaths in up to 7 years of follow-up, and the event rate (MVR or repeat CBC) was 10% (Figure 3B)7 in patients who after CBC had MVA ≥1.5 cm² and mean PA wedge pressure ≤18 mm Hg.

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have moderate or severe increase of pulmonary vascular resistance.

It is important to recognize that if the conditions exist for CBC and/or surgical valve repair, performing MVR is inappropriate because MVR is associated with a higher hospital and late mortality and a higher complication rate related to the prosthesis.

**Indications for CBC in Asymptomatic Patients With MS**

The MVA should be 
\[
\frac{1}{10.22} \text{cm}^2 \\
\frac{1}{1.0} \text{cm}^2,
\]

or 1.0 to 1.5 cm² in selected patients, the valve should be suitable for CBC, there should be no contraindications for CBC, and appropriate skill and experience with CBC should be available. The indications are:

- pulmonary arterial hypertension
- episodic acute pulmonary edema
- atrial fibrillation/flutter (paroxysmal/permanent)
- embolism (systemic/pulmonary) and no thrombus in LA/ inferior vena cava
- contemplating future pregnancy
- occupations that pose high risk to patient/public

**Special Situations**

**Mitral Regurgitation**

Grade ≤2/4 MR is not a contraindication. After CBC, MR may be eliminated in some patients if valve morphology is very favorable (USC score of 0 to 1).7

**Calcium in Commissures**

Presence of the Ca²⁺ in only 1 commissure makes it possible to get a reasonable result with CBC.10

**High Echo Scores**

With echo scores of 9 to 16 (MGH) or 3 to 4 (USC), the result with CBC will not be excellent. A patient in NYHA FC III and possibly also FC IV with an echo score of 9 to 11 (MGH) or 3 (USC), however, may obtain symptomatic benefit for a number of years with CBC before MVR becomes necessary.10

**LA Thrombus**

A mobile or free-floating thrombus in LA is a contraindication to CBC. Thrombus present only in the atrial appendage is usually not a contraindication to CBC for skilled and experienced personnel if echocardiography is used during the procedure. Other patients with LA thrombus should have 3 to 6 months of warfarin therapy (international normalized ratio 2 to 3), after which CBC can be undertaken if the thrombus is no longer present.

**Associated Significantly Obstructive Coronary Artery Disease**

If coronary lesions are amenable to percutaneous catheter interventions, these can be combined with CBC. Various combinations of catheter interventions and surgery may be feasible.
Aortic Regurgitation and Previous Surgical Commisurotomy

Aortic regurgitation and previous surgical commissurotomy are not contraindications.

Pregnancy

Patients who have severe MS, are asymptomatic, or are symptomatic but are contemplating pregnancy should have CBC before pregnancy. If the patient with moderate to severe MS is already pregnant and the symptoms cannot be controlled with medical therapy, then CBC can be performed while protecting the fetus from radiation as best as one can. This requires total abdominal and pelvic shielding and a reduction in the need for fluoroscopy with use of echocardiography during CBC in the catheterization laboratory.

Contraindication to Transseptal Catheterization

Retrograde nontransseptal CBC using the arterial approach can be performed in centers with skilled and experienced physicians. In such centers, the results are similar to those obtained with antegrade transeptal CBC.

Mild MS

CBC has been performed in patients with mild MS (MVA >1.5 to 2.0 cm²). The favorable natural histories of patients with mild MS at least over 10 years indicate that CBC is inappropriate in these patients. There are special circumstances when it should be considered, however. For example, in patients with elevated LVDP that cannot be controlled with medical or interventional therapy and who are significantly symptomatic from elevated pulmonary (venous and/or arterial) hypertension, CBC can be performed in the hope that by increasing the MVA to >2 cm² the pulmonary (venous and/or arterial) hypertension will be reduced and the symptoms will be relieved or improved. Also, it may be considered as a part of a prospective randomized trial that has adequate power.

Addendum

Months after submission of our manuscript, Palacios and coworkers published long-term outcomes (follow-up mean 4.2±3.7 years; range: 0.5 to 15) after CBC in 879 patients. The hospital mortality was 1.9% and incidence of in-hospital MVR was 3.8%; on follow-up, mortality was 13%, MVR and re-do CBC were needed in 27.7% and 6.4%, respectively, and 47.2% had events.

The outcomes on the basis of the MGH echo scores of ≤8, 9 to 11, and ≥12 are shown in Figure 5. To diagnose a left-to-right shunt, they have used the criterion of a step-up of O₂ saturation of ≥7%, which would exclude all atrial septal defects with Q/Qs <1.5:1. This will overestimate systemic flow by up to 40%, which will result in calculation of a MVA that is also overestimated. They have reported only shunts of with Q/Qs of ≥1.5:1. Also, they have calculated the MVA by the older Gorlin formula and not one modified by Gorlin.

References

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