REVIEW

Evaluation of mitral stenosis in 2008

Évaluation du rétrécissement mitral en 2008

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KEYWORDS
Mitral stenosis; Mitral valve area; Mitral valve morphology; Percutaneous mitral valve commissurotomy

Summary
Percutaneous mitral valve commissurotomy (PMC) is the treatment of choice for patients with mitral stenosis (MS) and favorable anatomy. Evaluation of MS should answer two questions: is MS severe? And is the valve suitable for PMC?

Evaluation of MS severity relies on accurate echocardiographic assessment of the mitral valve area (MVA). Several methods can be used, often in combination. The planimetry is the reference method but must be precisely performed at the tips of the leaflets in a well-oriented plane and thus requires experienced operators. New imaging technologies, such as 3D-echocardiography, MRI or computed tomography may reduce planimetry’s operator dependence. The pressure half-time method (PHT) has the merit of simplicity but should be used cautiously in elderly patients or those in atrial fibrillation. It is invalid immediately after PMC but can still be used as a semi-quantitative method: a PHT less than 130 msec is associated with a good valve opening with an excellent specificity and positive predictive value whereas a PHT 130 msec does not allow any conclusion. The continuity equation, easy to perform, may be invalidated by the commonly associated aortic or mitral regurgitation or in case of atrial fibrillation. The PISA method, is reputed technically challenging and requires a direct measurement of angle between the mitral leaflets, although the use of a fixed value of 100° provides an accurate MVA estimation. The main indication of transesophageal echocardiography is the exclusion of left atrial thrombus, which is a contra-indication to PMC as well as a 2/4 or greater mitral regurgitation grade.

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Two-dimensional-echocardiography allows detailed evaluation of valve morphology, including leaflet thickness and mobility, degree and localization of calcifications, extent of the subvalvular involvement. Unfavorable valve anatomy is associated with a lower rate of PMC success and lower event-free survival. However, given the low predictive value of all anatomic scores, the decision to perform or not the procedure should be based on a global approach taking into account not only the valve anatomy but also individual patients characteristics such as age, rhythm, NYHA class, MVA and the predicted operative mortality based on associated comorbidities.

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Abbreviations

CT = Computed tomography
LVOT = Left ventricular outflow tract
MRI = Magnetic resonance imaging
MSCT = Multi-slices computed tomography
MS = Mitral stenosis
MVA = Mitral valve area
NYHA = New York Heart Association
PHT = Pressure half-time
PISA = Proximal isovelocity surface area
PMC = Percutaneous mitral valve commissurotomy
3-D = Three-dimensional
TVI = Time-velocity integral
2-D = Two-dimensional

Introduction

The principal cause of MS is rheumatic heart disease. Despite a striking decrease in the prevalence of rheumatic fever, MS remains a significant problem in Western countries, accounting for 12% of native valvular heart disease, partially due to immigration from developing countries [1]. The clinical presentation of MS has changed, however; nowadays, it tends to affect older patients with mitral valve calcification. In developing countries, rheumatic fever remains endemic, and MS is a major public health problem.

In contrast to other valvular disease (with the exception of aortic stenosis, for which percutaneous valve replacement is an emerging option), surgery is not the only treatment strategy for MS. Since its introduction by Inoue...
et al. in 1984 [2], PMC has been performed successfully and safely in large series of patients at numerous centres [3–7], and has emerged as the treatment of choice for patients with MS and a favourable anatomy [8,9]. Nowadays, echocardiography plays a key role in the assessment of MS severity and anatomy, and catheterization is used only rarely. The evaluation of MS should answer two questions: is the MS severe and is the valve suitable for PMC? In this review, we discuss the evaluation of patients with MS in 2008, underlining the potential role of new technologies such as CT, MRI and 3-D echocardiography.

**Evaluation of MS severity**

The management of patients with MS relies on the accurate assessment of MS severity. MVA is the main criterion, with clinically-significant MS defined as an MVA less or equal to 1.5 cm² [9]. In some patients, it may be useful to take body size into account; there is general agreement that MS is significant if the MVA is less than 0.9 or 1 cm²/m² of body surface area. The mean transmitral gradient, determined from the transmitral velocity curve, is less useful because of its dependence on heart rate, rhythm and cardiac output, but it can still be regarded as an indicator and is an important prognostic factor. As cardiac catheterization is used typically to perform PMC, MVA is most often measured non-invasively by Doppler echocardiography, for clinical decision-making. Four different methods can be used: planimetry, PHT, continuity equation and PISA. Each method has its specific limitations. We use planimetry preferentially in our clinical practice, but a combination of methods is recommended for less experienced operators or in difficult clinical situations, to improve the consistency and reliability of MVA measurements.

**Planimetry**

Planimetry provides an anatomical measurement of the mitral valve orifice; it is considered to be the reference method and correlates closely with anatomical findings [10,11]. Planimetry is performed in parasternal short-axis view, precisely at the tips of the leaflet in a well-orientated plane (Fig. 1). The procedure requires an experienced operator because minor changes to the depth or angle of the ultrasound beam may lead to significant MVA overestimation [12]. To avoid such overestimation, it is important to scan slowly from the apex to the base and to select the narrowest orifice. Planimetry may not be feasible in approximately 5% of patients because of a poor echocardiographic window or massive calcifications [6]. Because of these limitations, other technologies have been evaluated, namely 3-D echocardiography, CT and MRI.

3-D echocardiography is a relatively recent imaging technique that permits the 3-D visualization of heart structures. With improvement of transducer technology (matrix array transducer), on-line 3-D acquisition, visualisation and analysis have become possible (real-time 3-D transthoracic echocardiography). The process allows the 3-D acquisition of the entire mitral valve, which can be sliced along any plane as desired, and thus overcomes a major limitation of 2-D echocardiography (Fig. 2) [13]. A recent study has shown that 3-D echocardiography provides better reliability than 2-D echocardiography among inexperienced operators (level I training in echocardiography) (Fig. 3), reflecting its greater accuracy in providing the image plane with the true orifice of the mitral valve [14]. This should be considered as a potential indication for 3-D echocardiography.

MSCT also enables the 3-D acquisition of the entire heart throughout the cardiac cycle and multiple plane reconstructions; like echocardiography, therefore, it can provide a parasternal short-axis view of the mitral valve orifice at the tips of the leaflet in early diastole (Fig. 4). We showed recently that accurate and reproducible planimetry of the mitral valve orifice could be achieved using a 16-detector-row scanner with commercially-available cardiac reconstruction software and contrast enhancement [15]. MSCT measurements correlated well with, and did not differ from, echocardiographic measurements; the mean difference was small and intra- and interobserver variability were low. In addition, acquisition of CT images depends on the protocol used, which can be preregistered in the CT system, and a step-by-step operations manual for plane orientations can then be produced, which may reduce the operators’ dependence on MSCT measurements. After brief training, an inexperienced operator (a radiology technologist with no previous experience in valvular disease) was asked to perform the measurements alone, and produced results that did not differ from those of experienced operators. It is worth noting that only patients in sinus rhythm were enrolled in this study. MSCT can therefore be considered as an alternative to MVA measurement in patients with poor echocardiographic windows or for teams unaccustomed to evaluating patients with MS. Because of the intrinsic limitations of MSCT (i.e. risk of irradiation and iodine contrast), we do not recommend this procedure as a first-intention method for the assessment of MS severity.

Preliminary results suggest that planimetry of the mitral valve orifice using MRI is feasible and reliable, despite some degree of overestimation of the MVA [16]. Velocity-encoded cardiovascular magnetic resonance may also facilitate calculation of the MVA using the PHT method [17].

**PHT**

The PHT is the time interval between the maximum early diastolic gradient and the point at which the gradient is half this maximum value. Since the original report by Hatle et al., based on only 32 patients [18], the PHT method has gained widespread acceptance, despite the lack of large-scale clinical validation [19,20] and theoretical concerns [21]. The main advantage of PHT is its simplicity (MVA = 220/PHT); consequently, it is used widely in clinical practice in addition to, or even instead of, planimetry. However, the important limitations of the PHT method should be emphasized.

Tachycardia and non-linear Doppler velocity curves affect the accuracy and reliability of PHT measurements [22,23]. The PHT method is also invalidated by severe aortic regurgitation. In addition, a major assumption of the PHT method is that the rate of pressure decline is only determined by
Figure 1. Examples of mitral valve anatomy. A. Thick valve without calcification. B. Planimetry of MVA in parasternal short-axis view. C. Flexible mitral valve in parasternal long-axis view. D. Calcification localized at the level of the medial commissures (small red arrow). E–F. Restenosis due to valvular rigidity with persistent commissural opening (large arrows).

In clinical practice, correlation between planimetry and PHT is only fair, with discrepancies greater than or equal to 0.3 cm² observed in 20% of patients [24]. The PHT method should be used with caution, especially in older patients or those in atrial fibrillation in whom the PHT may be highly variable from beat to beat. This limitation is of critical importance in Western countries where the mean age of patients with MS is almost twice that observed in developing countries, and where one third to one half of patients with MS are in atrial fibrillation. Furthermore, because of acute atrioventricular compliance changes, the PHT method is reputed invalid immediately after PMC [21]. In our experience, the PHT method does not provide an accurate evaluation of the MVA after PMC: the correlation with planimetry is weak, the mean difference is large and a discrepancy greater than or equal to 0.3 cm² is noted in almost 50% of patients [24]. However, it can still be used as a semiquantitative method and provides an additional tool for the evaluation of MVA after PMC in difficult cases. A PHT less than 130 ms is associated with a good valve opening (MVA ≥ 1.5 cm²) with excellent specificity and a positive predictive value, whereas a PHT greater than or equal to 130 ms does not enable any conclusions to be drawn.

Continuity equation

The continuity equation is based on the conservation of blood flow across the LVOT and the mitral valve (Fig. 5). The MVA is calculated as the ratio of the aortic stroke volume to the mitral TVI obtained by continuous-wave Doppler. The continuity equation is quite simple to calculate but is invalidated by aortic or mitral regurgitation, which are often associated with MS [11]. In addition, as mitral and aortic stroke volumes are calculated from different beats,
Figure 2. Measurement of MVA using real-time 3-D echocardiography. The 3-D volume (D), acquired in parasternal short-axis view, is sliced and orientated to obtain the ideal cross-section of the mitral valve at the tips of the leaflets (A–C).

the continuity equation should be used cautiously in cases of atrial fibrillation; the results from 5–10 beats must be averaged. Overall, the continuity equation provides smaller measurements than planimetry, especially after PMC (functional versus anatomical orifice area).

PISA

The PISA method is based on the continuity principle [25] and assumes that blood flow converging towards a flat orifice forms hemispheric isovelocity shells. The

Figure 3. Bland–Altman analysis shows better agreement between (B) 3-D planimetry measured by the less experienced operator and 2-D planimetry measured by the experienced operator than between (A) 2-D planimetry measured by less experienced and experienced operators.
Figure 4. Examples of parasternal short-axis views of the mitral valve orifice obtained by MSCT (with contrast injection; white and black colours are inverted so that images appear similar to echocardiography). A, B. Commissures are fused in the first patient. C. Both commissures are open. D. Only the lateral commissure is open.

Figure 5. Calculation of the MV A (red arrow) using the continuity equation.

PISA method is used routinely in many echocardiography laboratories for the quantitative evaluation of valvular regurgitation [26]. Many studies have validated the PISA method for the calculation of MVA in patients with MS, under a variety of clinical conditions (including differing heart rhythms and severities of anatomical lesions, and with associated aortic or mitral regurgitation) [25,27,28], but it is still used rarely in routine practice. The PISA method is a useful tool in patients with MS because the proximal convergence method can be visualized easily and it may be the only method available. It is reputed to be technically demanding, but this is not the case if the following rules are adhered to:

- zoom on the flow convergence;
- upshift the baseline velocity and use an aliasing velocity of 20–30 cm/s;
- measure the radius of the flow convergence region and the transmitral velocity at the same time in early diastole;
- measure the $\alpha$ angle formed by the mitral leaflets.

As a result of leaflet doming in MS, only a fraction of a hemisphere crosses the orifice and an angle correction factor ($\alpha$) must be considered (Fig. 6). This angle cannot be obtained using the machine’s built-in software and must be measured manually using a protractor. This issue may explain, at least partially, why the use of the PISA method remains limited in MS. However, the angle changes only slightly between patients and the use of a fixed angle value of 100$^\circ$ can provide an accurate MVA estimation in patients with MS [29]. This simplification should facilitate and extend the use of the PISA as an additional method for the assessment of MS severity in routine practice.

Colour M-mode PISA allows instantaneous measurement of MVA throughout diastole (Fig. 7) and has shown that despite marked flow and velocity changes during diastole, the MVA remains unchanged, irrespective of the severity of mitral anatomical alterations or the presence of mitral regurgitation [28].
Assessing the consequences of MS

Size of left atrium

Left atrial enlargement is caused by chronic pressure overload. M-mode measurement is simple but inaccurate because the left atrium does not enlarge symmetrically. In both mitral regurgitation [30] and MS (personal unpublished data), the M-mode diameter estimates left atrial volume imprecisely, with a wide range of error that increases with left atrial size. Hence left atrial area — or, for better, left atrial volume — should be used to estimate left atrial size.

Anticoagulation is recommended for patients in sinus rhythm with a left atrial diameter greater than 50 mm [9]. It is evident that more precise area or volume thresholds are clearly needed.

Systolic pulmonary artery pressure

Increased left atrial pressure results in pulmonary venous hypertension. A systolic pulmonary artery pressure greater than 50 mmHg at rest is accepted as an indication for PMC [9]. Stress echocardiography (exercise or dobutamine echocardiography) may be helpful in the management of asymptomatic patients with MS [31,32]. Exercise echocardiography can uncover symptoms and reduced functional capacity. A systolic pulmonary artery pressure greater than 60 mmHg on exercise has been proposed as an indication for PMC [9]. However, prospective studies are mandatory to validate this threshold and the predictive value of stress echocardiography with regard to outcome; our preliminary experience suggests that a rapid rise in pulmonary artery pressure may be more informative than the peak pulmonary artery pressure.

Size of right-side chambers and degree of tricuspid regurgitation

The sizes of the right-side chambers of the heart are a reflection of left atrial and pulmonary venous hypertension. Tricuspid regurgitation is often associated with MS and is mostly functional; it usually decreases or resolves after PMC [33], but severe tricuspid regurgitation is a risk factor for poor long-term PMC outcome.
Table 1: Anatomical classification of the mitral valve: Wilkins’s score.

| Leaflet mobility  | 1. Highly mobile valve with restriction of only the leaflet tips |
|                  | 2. Middle portion and base of leaflets have reduced mobility |
|                  | 3. Valve leaflets move forward in diastole mainly at the base |
|                  | 4. No or minimal forward movement of the leaflets in diastole |
| Valvular thickening | 1. Leaflets near normal (4—5 mm) |
|                   | 2. Mid-leaflet thickening, marked thickening of the margins |
|                   | 3. Thickening extends through the entire leaflets (5—8 mm) |
|                   | 4. Marked thickening of all leaflet tissue (8—10 mm) |
| Subvalvular thickening | 1. Minimal thickening of chordal structures just below the valve |
|                     | 2. Thickening of chordae extending up to one third of chordal length |
|                     | 3. Thickening extending to the distal third of the chordae |
|                     | 4. Extensive thickening and shortening of all chordae extending down to the papillary muscle |
| Valvular calcification | 1. A single area of increased echo brightness |
|                        | 2. Scattered areas of brightness confined to leaflet margins |
|                          | 3. Brightness extending into the mid-portion of leaflets |
|                           | 4. Extensive brightness through most of the leaflet tissue |

Table 2: Anatomical classification of the mitral valve: Cormier’s score.

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<th>Echocardiographic group</th>
<th>Mitral valve anatomy</th>
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<tr>
<td>Group 1</td>
<td>Pliable non-calcified anterior mitral leaflet and mild subvalvular disease, i.e. thin chordae $\geq 10$ mm in length</td>
</tr>
<tr>
<td>Group 2</td>
<td>Pliable non-calcified anterior mitral leaflet and severe subvalvular disease, i.e. thickened chordae $&lt; 10$ mm in length</td>
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<tr>
<td>Group 3</td>
<td>Calcification of mitral valve of any extent, as assessed by fluoroscopy, whatever the subvalvular apparatus</td>
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Suitability for PMC

**Mitral valve morphology**

2-D echocardiography allows detailed evaluation of valve morphology, including leaflet thickness and mobility, degree and localization of calcifications, and the extent of the subvalvular involvement (Fig. 1). Several scoring systems have been proposed. The method used most widely was developed at the Massachusetts General Hospital [34]: four features (leaflet mobility, leaflet thickening, subvalvular thickening and calcification) are scored on a 1–4 scale and the total score is obtained by adding each of the component scores (Table 1). An unfavourable anatomy, defined by a score greater than 8, is associated with a lower rate of immediate PMC success and a lower event-free survival rate. However, this scoring system is complex and subjective. In our institution, we use Cormier’s method, which is the simplest scoring system (Table 2). However, all the proposed systems have a poor predictive value and no direct comparisons between systems are available.

The presence and extent of valvular calcification is an important prognostic factor for long-term outcome, although a number of other factors (such as age, heart rhythm, NYHA class and valve area [35]) must also be taken into consideration. Patients should not be denied PMC solely on the basis of an unfavourable anatomy, as good immediate and midterm results can be achieved in patients with unfavourable anatomy – even those with valvular calcification [35,36]. It is important to underline that none of the scoring systems accounts for the location of the calcification, especially relative to the commissures [37,38].

**Restenosis after previous commissurotomy**

Restenosis can occur after commissurotomy as a result of commissural refusion or valve rigidity with persistent commissural opening (Fig. 1). PMC should not be considered in the latter case, but can produce satisfactory results in patients with commissural refusion and favourable anatomy – particularly in young patients with no or mild calcification.

Table 3: Contraindications to percutaneous valve commissurotomy [9].

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<th>Condition</th>
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<td>MVA $\geq 1.5$ cm$^2$</td>
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<tr>
<td>Left atrial thrombus</td>
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<tr>
<td>Mitral regurgitation that is more than mild (grade $\geq 2$)</td>
</tr>
<tr>
<td>Severe or bicommissural calcification</td>
</tr>
<tr>
<td>Absence of commissural fusion</td>
</tr>
<tr>
<td>Severe concomitant aortic valve disease or severe combined tricuspid stenosis and tricuspid regurgitation</td>
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<tr>
<td>Concomitant coronary artery disease requiring bypass surgery</td>
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</table>
Evaluation of mitral stenosis in 2008

Figure 8. Assessment of commissural opening using real-time 3-D echocardiography. Parasternal short-axis view from ventricular perspective: en face, medial and lateral views of a patient with complete bilateral commissural opening.

Mitral regurgitation

The detection and quantification of the degree of mitral regurgitation has important implications for the choice of intervention. A mitral regurgitation grade greater than or equal to 2 is considered to be a contraindication to PMC (Table 3). However, in patients with borderline mitral regurgitation, PMC is more likely to be performed if the valve anatomy is favourable.

Left atrial thrombus

Left atrial thrombi are usually (but not exclusively) located in the left appendage [41]. The diagnosis relies on transoesophageal echocardiography, which has high sensitivity and specificity for the detection of left atrial thrombus. This is the major indication for the use of transoesophageal echocardiography, as almost all other variables can be assessed by transthoracic echocardiography. Transoesophageal echocardiography should only be performed immediately before PMC (or surgery). Although an important thromboembolic risk factor, left atrial dense spontaneous contrast (unlike left atrial thrombus) is not a contraindication to PMC and is a IIa indication in asymptomatic patients.

Conclusion

An evaluation of MS should determine if the MS is severe and whether the valve is suitable for PMC. Assessment of MS severity relies on accurate echocardiographic measurement of the MVA. Planimetry remains the reference method, but is operator-dependent; the use of a combination of other methods (PHT, continuity equation and PISA) is recommended for less experienced operators or in difficult clinical situations. 3-D echocardiography and CT seem promising and may decrease planimetry’s operator dependence. The PISA method is used rarely in routine practice, but ought to be implemented more widely as it may be the only method available and can be simplified by using a fixed angle value of 100° between the valve leaflets. Unfavourable valve anatomy is associated with a lower rate of PMC success and a lower event-free survival rate. However, given the low predictive value of the various anatomical scoring systems for PMC outcome, the decision to perform the procedure should take into account not only the valve anatomy but also individual patient characteristics, such as age, heart rhythm, NYHA class and valve area, and predicted operative mortality based on associated comorbidities.

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