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Review Article

The 40th Anniversary of Percutaneous Balloon Valvuloplasty for Mitral Stenosis: Current Status

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ABSTRACT

Percutaneous balloon mitral valvuloplasty (PBMV), once the most complex of percutaneous cardiac procedures and essentially the first adult structural heart intervention, set the stage for a host of new technologies. Randomized studies comparing PBMV to surgery were the first to provide a high-level evidence base in structural heart. The devices used have changed little in 40 years, but the advent of improved imaging and the expertise gained in interventional cardiology has provided some additional procedural safety. However, with the decline in rheumatic heart disease, PBMV is being performed in fewer patients in industrialized nations; in turn, these patients have more comorbidities, less favorable anatomy, and thus a higher rate of procedure-related complications. There remain relatively few experienced operators, and the procedure is distinct enough from the rest of the structural heart intervention world that it has its own steep learning curve. This article reviews the use of PBMV in a variety of clinical settings, the influence of anatomic and physiologic factors on outcomes, the changes in the guidelines, and alternative approaches. PBMV remains the procedure of choice in patients with mitral stenosis with ideal anatomy and a useful tool in patients with less than ideal anatomy who are poor surgical candidates. In the 40 years since its first performance, PBMV has revolutionized the care of mitral stenosis patients in developing countries and remains an important option for suitable patients in industrialized nations.

ABBREVIATIONS

ARF, acute rheumatic fever; DOAC, direct oral anticoagulant; LAA, left atrial appendage; MAC, mitral annular calcification; MR, mitral regurgitation; MS, mitral stenosis; MVD, mitral valve disease; PBMV, percutaneous balloon mitral valvuloplasty; PHT, pulmonary hypertension; RCT, randomized controlled trial; RHD, rheumatic heart disease; SHD, structural heart disease; TAVR, transcatheter aortic valve replacement; TEE, transesophageal echo; TEER, transcatheter edge to edge repair; TTE, transthoracic echocardiogram.

Introduction

Percutaneous balloon mitral valvuloplasty (PBMV) was, at the time of its introduction (1982, published in 1984), the most complex interventional procedure in adult cardiology.[1] Reliant on transseptal puncture techniques that were in evolution and primitive wire and balloon technology, it featured a steep learning curve superimposed on a background of limited imaging and little to no operator experience with percutaneous structural heart interventions. Interest in the procedure was only modest: rheumatic heart disease (RHD), once the primary cardiac diagnosis for hospital admissions worldwide, had receded into the low single-digit percentages of heart disease diagnosis in the industrialized world, although still highly prevalent in developing countries.[2] As rheumatic mitral stenosis (MS) is primarily seen by health care systems with highly strained financial resources, there was and remains little incentive for industry to develop devices targeted specifically to its treatment.

Against this background, a series of randomized controlled trials (RCTs) demonstrated the noninferiority and subsequently superiority of PBMV compared with surgery for rheumatic MS when the anatomy is favorable.[3-6] At the time of these studies, not a single RCT of surgery for any type of valvular heart disease had been performed; thus, these were pioneering efforts in a research pathway that has become well established with large RCTs accompanying the introduction of transcatheter aortic valve replacement (TAVR) and mitral transcatheter edge to edge repair (TEER). Cardiologists in developing countries still perform PBMV in high volumes, but relatively few operators in industrialized nations

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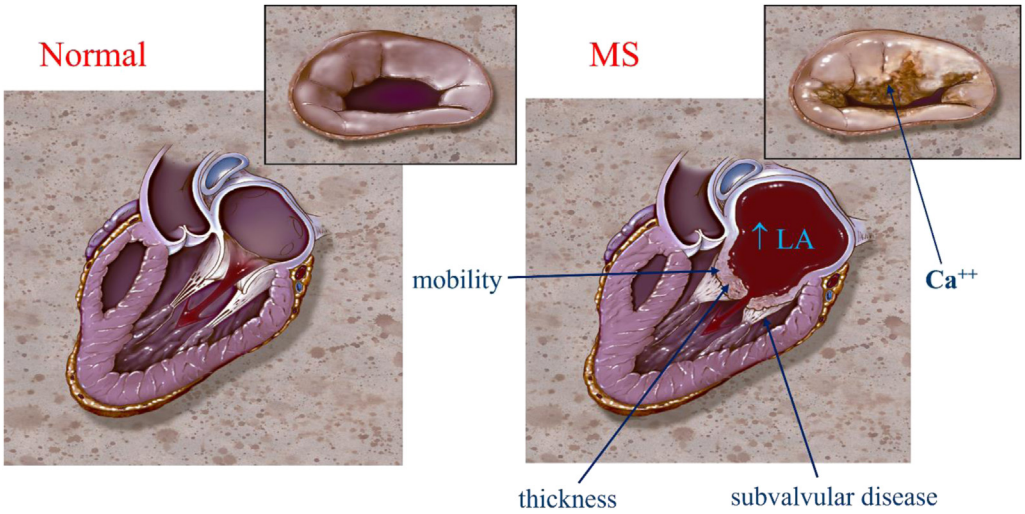

Figure 1. The normal mitral valve on the left and with mitral stenosis on the right. Note the characteristic features of mitral valve leaflet thickening, restricted mobility (classic hockey stick configuration, subvalvular shortening and thickening, and calcification of the leaflets) seen in rheumatic heart disease. The left atrium is dilated; with mitral stenosis and atrial fibrillation there is commonly blood stasis, sometimes seen as swirling contrast by echo (spontaneous echo contrast). From Turi ZG. Cardiology patient page. Mitral valve disease. Turi Z. *Circulation* 2004, 109:e38-e41.
Abbreviations: Ca++, calcification; LA, left atrium; MS, mitral stenosis.

have significant training or experience. During the 4 decades since the first PBMV, structural heart disease (SHD) interventions overall have had explosive growth, whereas PBMV now plays only a small role. It nevertheless remains an important therapeutic tool for rheumatic MS, and although less complex than many of the newer SHD procedures, it has elements that are unique and, as such, requires experience and judgment for safe performance as well as understanding of hemodynamic subtleties.[7,8] The 40-year history of the technique has allowed for significant understanding of the natural course of treated MS, the long-term effects of PBMV, the impact of ancillary manifestations of MS on cardiac pathology including pulmonary hypertension (PHT), left ventricular (LV) and right ventricular (RV) dysfunction, and atrial arrhythmias. Although the techniques and technology have had relatively little evolution since 1982, dramatic improvements in imaging have taken place. This article reviews the current status of PBMV, the evolution of the evidence base, the revisions of the guidelines, and newer insights into outcomes.

Rheumatic Mitral Stenosis

MS is predominantly the result of postrheumatic deformity. There is an initial inflammatory process, valvulitis, associated with rheumatic carditis that typically manifests as mitral regurgitation (MR), with subsequent scarring, thickening and calcification of the valve leaflets, fusion of the commissures, and leaflet immobility with chordal involvement of the subvalvular apparatus. The obstruction to outflow from the left atrium can be at multiple levels: the leaflets themselves are the primary source, but in addition, a gradient can result from narrowing of the subvalvular apparatus or the mitral annulus; in advanced disease, it may involve all 3. The consequent pressure overload of the left atrium results in left atrial enlargement and atrial fibrillation, PHT, right heart failure, and stasis of blood with embolic stroke. Figure 1 shows the anatomy of the mitral valve and cardiac chambers in isolated pure MS.

RHD occurs early in life in developing countries. Children who are untreated for acute Group A beta-hemolytic streptococcal pharyngitis and develop acute rheumatic fever (ARF) frequently go on to significant cardiac pathology by their 20s and 30s, although the age range is highly variable; the author has seen end-stage rheumatic heart disease in a 9-year-old. The occurrence of multiple bouts of pharyngitis (and occasionally streptococcal cellulitis) with ARF is particularly likely to precipitate early significant symptomatic valvular disease. The predominant cardiac pathology associated with RHD involves the mitral valve, although a significant minority have concomitant aortic valve involvement (in the range of 20%-30%), with aortic insufficiency most common in this subset. Isolated aortic valve involvement is uncommon (and isolated aortic stenosis rare). Concomitant rheumatic tricuspid disease typically manifests as tricuspid regurgitation, while severe rheumatic tricuspid stenosis is also rare.[9]

Characteristic presentation of MS in developing countries is during pregnancy in young women because of the effect of increased intravascular volume and high transvalvular flow rates typical during gestation. The disease is less common in men who in developing countries may experience onset of symptoms with hard physical labor. In industrialized nations, where aggressively rheumatogenic strains of Group A beta-hemolytic *streptococcus* are less prevalent and recurrent bouts of rheumatic fever are rare, the disease is more commonly diagnosed in patients in their 40s and beyond. These patients frequently have comorbidities, and the disease is frequently not diagnosed until an echocardiogram is obtained, in part because of the unfamiliarity of most clinicians in the West with MS and the consequent waning of the required diagnostic skills. The natural course of the disease was well studied before the advent of definitive therapy and includes PHT, onset of atrial fibrillation, progressive disability, and eventual death with right and left heart failure, stroke and, in particular when there is mixed valve disease, end-stage cardiomyopathy. One-year mortality of MS in New York Heart Association Class IV patients was >50% in the presurgical era.[10] Although ARF remains a significant public health issue in developing countries, its incidence is declining even there[11]; RHD is seen in industrialized nations primarily in immigrants from endemic areas, those with poor access to basic health care, and in an older population who were exposed to streptococcal infections before the modern antibiotic era.

Nonrheumatic Mitral Stenosis

Calcification of the leaflets and/or mitral annulus occurring in patients without RHD is a degenerative process seen in association with comorbidities,[12] including chronic kidney disease with its attendant elevated parathyroid hormone levels, diabetes, and coronary artery disease.[13] Uncommonly, MS may be related to congenital, eosinophilic, or carcinoid heart disease and rarely, secondary to radiation; these causes of mitral obstruction typically do not include commissural fusion[14] hence PBMV is unlikely to be beneficial. However, calcification of the mitral leaflets, subvalvular apparatus, and, in particular, the annulus in these nonrheumatic subsets results in obstruction of flow and can be confused with rheumatic MS, although the characteristic anatomic features in Figure 1 will be missing. In contrast, the echoes seen in Figure 2 (center and right) show absence of rheumatic deformity but extensive calcification of the annulus and leaflets. Balloon dilatation is largely appropriate only for rheumatic MS; the ability of balloons to effect significant anatomic and physiologic improvement for nonrheumatic calcified leaflets or annuli is limited, although there is some experience, to be

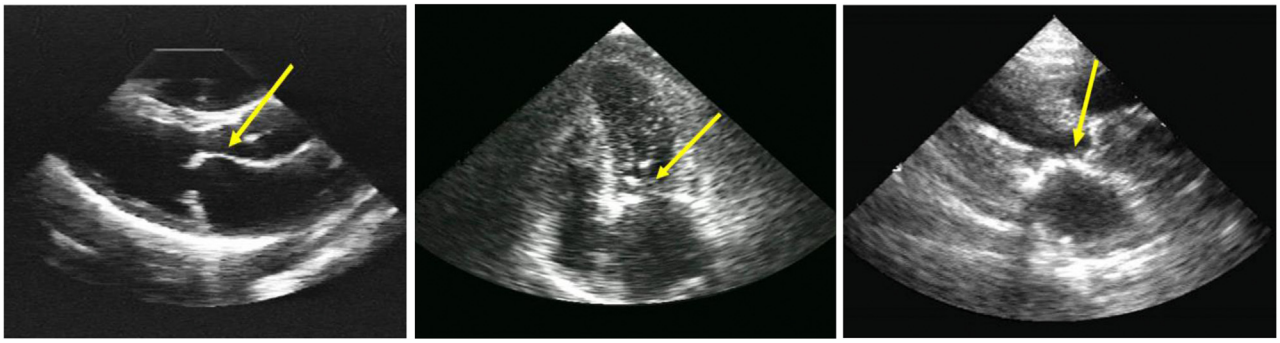

Figure 2. Image at left is parasternal long axis view of a patient with classic hockey stick deformity of the anterior mitral valve leaflet (arrow) and restricted mobility of the posterior leaflet. Center and right: apical and parasternal long axis views showing severe leaflet and annular calcification, respectively (arrows) in a 42-year-old patient with renal failure on dialysis. No rheumatic deformity is seen.

discussed subsequently, but alternative techniques involving percutaneous valve replacement now dominate this arena.[15]

Evaluation

History and Physical Examination

Patients presenting with significant MS frequently (~50%) have no recollection of having had ARF. Patients typically complain of fatigue and occasionally palpitations, shortness of breath sometimes with wheezing, and are commonly misdiagnosed (and treated) for bronchospasm. Although bronchodilators produce some relief, the presence of catecholaminergic agents, which raise the heart rate, can be quite deleterious and potentially precipitate pulmonary edema. Patients can present with systemic embolism or embolic stroke as the first symptom. The physical examination of patients with MS includes assessment for an opening snap and S2-opening snap interval (experienced auscultators can judge intervals less than 100 msec, suggestive of severe MS), quality of the opening snap, and length of murmur extending throughout mid and late diastole. The continued presence of sinus rhythm does not exclude severe MS. Evaluation for PHT includes palpation for an RV lift and for a palpable and loud P2, an exaggerated A2-P2 interval, pulmonic and tricuspid regurgitation murmurs, and the typical signs of right heart failure. Particularly useful for the evaluation of patients being considered for MS intervention is a displaced point of maximum pulsation and LV heave; both indicate significant left-sided regurgitation, in particular mixed mitral valve disease (MVD) and/or aortic insufficiency; the isolated MS patient should have a small ventricle because of chronic underfilling of the LV. The nature of the first heart sound can provide important insights into the severity of MS as well as progression of disease of the valve leaflets and subvalvular apparatus. A loud first heart sound correlates with a gradient through end diastole, implying that the valve leaflets are still open as LV contraction begins and the valve closes abruptly. In contrast, as the leaflets become more rigid with worsening MS, the first heart sound may become muted; a diminished S1 can also be an important marker of progressive subvalvular disease, which in turn is an important consideration in judging suitability for PBMV.

Echocardiography

The mainstay of screening for PBMV remains the transthoracic echocardiogram (TTE).[14] TTE is the first pass technique for characterizing valve anatomy, including degree of thickening and calcification of the leaflets and subvalvular apparatus, severity and symmetry of commissural fusion, determination of gradient by Doppler, assessment of pressure half-time, and planimetry of the valve area. Any consideration of gradient should be in the context of heart rate and presence of MR; fast heart rate as well as significant MR will both result in higher gradient for any given degree of MS. The gradient, and the patient's symptoms as well, can also be significantly affected by conditions that result in a high output state (and thus high transvalvular flow): in specific pregnancy, fever, thyrotoxicosis, anemia, and from a practical standpoint undersedation during any procedure. TTE will also allow characterization of the right heart, extent of PHT, and concomitant aortic or tricuspid disease. Serial TTE when following patients with MS can be helpful in decision-making as to when to consider intervention: signs of increasing right heart stress (PHT, RV dilatation and dysfunction), progressive left atrial dilatation, and onset of atrial tachyarrhythmias. The severity of PHT and signs of right heart failure are highly significant; PHT is frequently reversible in young patients with severe MS, but this is less predictable in older patients where the pulmonary circulation is more likely to have undergone irreversible changes.

For patients whose TTE findings confirm the severity of MS and potential suitability for PBMV, a transesophageal echo (TEE) is essential: it provides additional insights into valve leaflet characteristics and is far more sensitive for diagnosis of 3 key confounders or relative contraindications: more than mild MR, spontaneous echo contrast in the left atrium, and clot in the left atrium including, in particular, the left atrial appendage (LAA; see discussion under Contraindications). It is important to consider the adequacy of sedation during TEE; tachycardia and hypertension from undersedation can have significant confounding effects on physiologic assessment of the severity of MVD, including the Doppler gradient, pressure half-time, and degree of MR. TEE is superior to TTE for visualization of the valve and commissures, severity and location of visualized MR, and valve area. Although planimetry is generally the procedure of choice, and in many cases can be done by TTE, there are several potential pitfalls. It requires good cross-sectional views, measurement at the correct plane of the valve annulus, properly judging the edges of the commissures, and under the best of circumstances has some degree of subjectivity on the part of the operator making the measurements; TEE and, in particular, 3D TEE can provide additional accuracy in mitral valve area determination. Two other modalities—computed tomography and cardiac magnetic resonance imaging—have been proposed as additional tools for assessing mitral valve anatomy.[14] The former allows concomitant assessment of coronary anatomy, whereas magnetic resonance imaging has been shown to have strong correlation with 3D echo evaluations.[16]

Echo Scores and Predictors of Outcomes

The primary technique used to assess the suitability for balloon dilatation remains the Wilkins-Weyman echo score, assigning a maximum of 4 points for each of leaflet calcification, subvalvular thickening, leaflet mobility, and leaflet thickness.[17] Each parameter ranges from 0 (normal) to 4 (severe disease) with total values of 8 or less considered ideal and >11 considered unfavorable.[18] A number of alternative scoring systems have been proposed because of multiple limitations of this score. First, only leaflet calcification and subvalvular

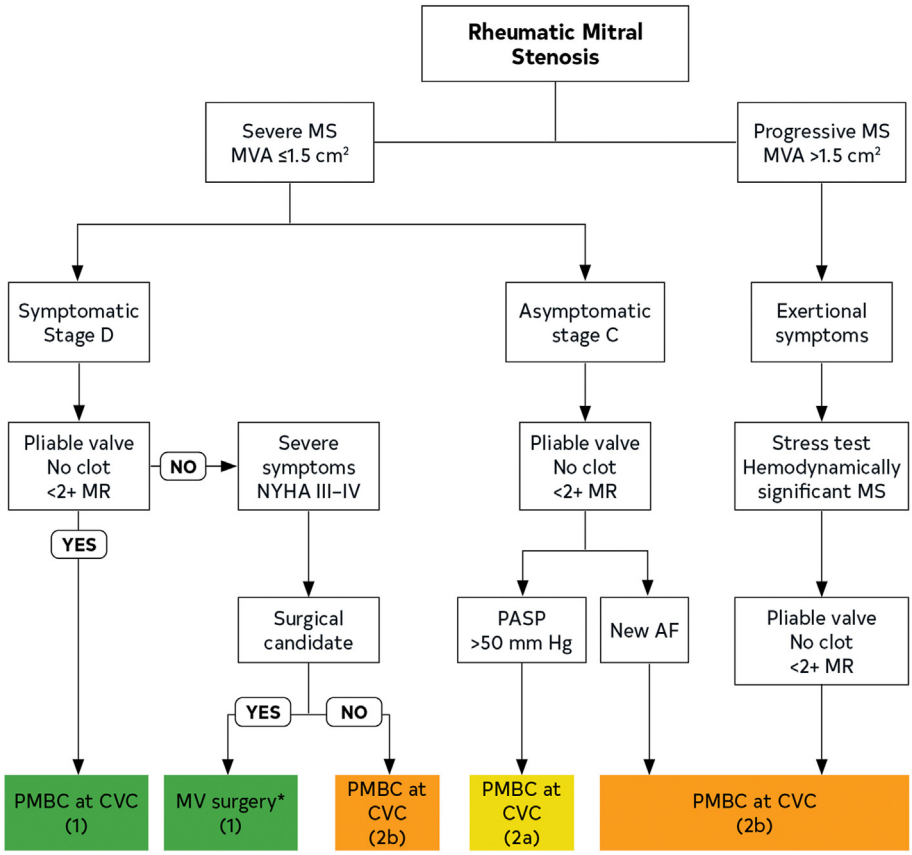

Figure 3. Algorithm for management of rheumatic mitral stenosis. From Otto CM, Nishimura RA, Bonow RO, et al. 2020 American College of Cardiology/American Heart Association guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2021; 77:e25-197.
*Repair, commissurotomy, or valve replacement.
Abbreviations: AF, atrial fibrillation; CVC, Comprehensive Valve Center; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; MVA, mitral valve area; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PMBC, percutaneous mitral balloon commissurotomy.

thickening are independently predictive of outcomes; leaflet mobility and leaflet thickening, the other 2 elements of the scoring system are not. Second, it does not provide discriminatory value predicting outcomes in patients in the middle range of 8 to 11. Third, a major limitation of the score is lack of consideration of the types and extent of commissural fusion; the effectiveness of balloon dilatation is largely predicated on the ability to split the commissures. Fourth, multiple factors correlate with the development of post-PBMV MR, including eccentrically fused or bilateral densely calcified commissures; in patients where most of the obstruction is at the level of the subvalvular apparatus, ballooning can result in disruption of the chordae and severe regurgitation as well. A number of alternative scoring systems have been proposed to separately predict the severity of MR postprocedure; however, severe MR is multifactorial, and accurate prediction requires taking into account anatomic features, including higher echo scores,[19] heavily calcified posterior leaflets,[20] dense eccentric or bilateral commissural fusion, and a severely thickened and calcified subvalvular apparatus.[21] More recent work on patients with leaflet tearing as a consequence of PBMV has shown that a particularly susceptible group are patients with uneven leaflet tissue density[22]; in our experience, these patients are younger, and the events are difficult to predict.

As most of the MS literature has used the Wilkins-Weyman scoring system, it remains the dominant means of characterizing suitability for PBMV. Although a threshold of >8 correlates with less favorable long-term outcomes,[18] it provides little insight into the "gray zone" between 8 and 11, and even patients with higher echo scores who are poor operative candidates should not be denied consideration of the procedure.[14] Because of its limitations, the guidelines only state "pliable valve, no clot" and no greater than mild MR rather than a score in the algorithm in Figure 3. One of several alternative scoring systems worthy of mention is by Nunes et al[21]; this adds the symmetry of commissural fusion reported as a commissural area ratio as well as leaflet displacement and reveals greater predictive value for outcome. Overall, multivariate predictors of short-term outcomes included post-PBMV mitral valve area, maximum leaflet displacement, commissural area ratio, and subvalvular thickening; multivariate long-term outcomes were predicted by age and the severity of postprocedure MR, gradient and mean pulmonary artery pressure. In general, there is a consensus that scores alone do not adequately predict outcome in individual patients and that a combination of anatomic features, demographics, and clinical findings should be applied.[14]

Exercise

If the patient's symptoms appear disproportionate to the severity of MS at rest, exercise can be helpful with its attendant increase in both heart rate and transvalvular flow. The disproportionate fall in diastolic filling period with increasing heart rate leads to substantial increases in gradient. The concomitant rise in pulmonary artery pressure to >60 mm Hg (although not formally incorporated in the guideline indications) and pulmonary wedge pressure to >25 mm Hg (Class 2b indication) with exercise have been used to assess patients for PBMV who otherwise have mild appearing MS.[23] Exercise during cardiac catheterization, as well as dobutamine and even temporary pacing can bring out significant increases in valve gradient (Figure 4).

Cardiac Catheterization

Once the mainstay of determining the severity of MS, cardiac catheterization has largely been superseded by noninvasive testing. When echo-derived data are equivocal, careful hemodynamic measurements in the cath lab can be diagnostic. In middle-aged and older patients, additional information can be gained on coronary anatomy (though coronary angiography is indicated only if patients are otherwise at risk for coronary artery disease based on age, gender, and comorbidities),[23] as well as direct measurement of right heart pressures and on occasion exercise hemodynamics while on the cath table. The calculation of pulmonary vascular

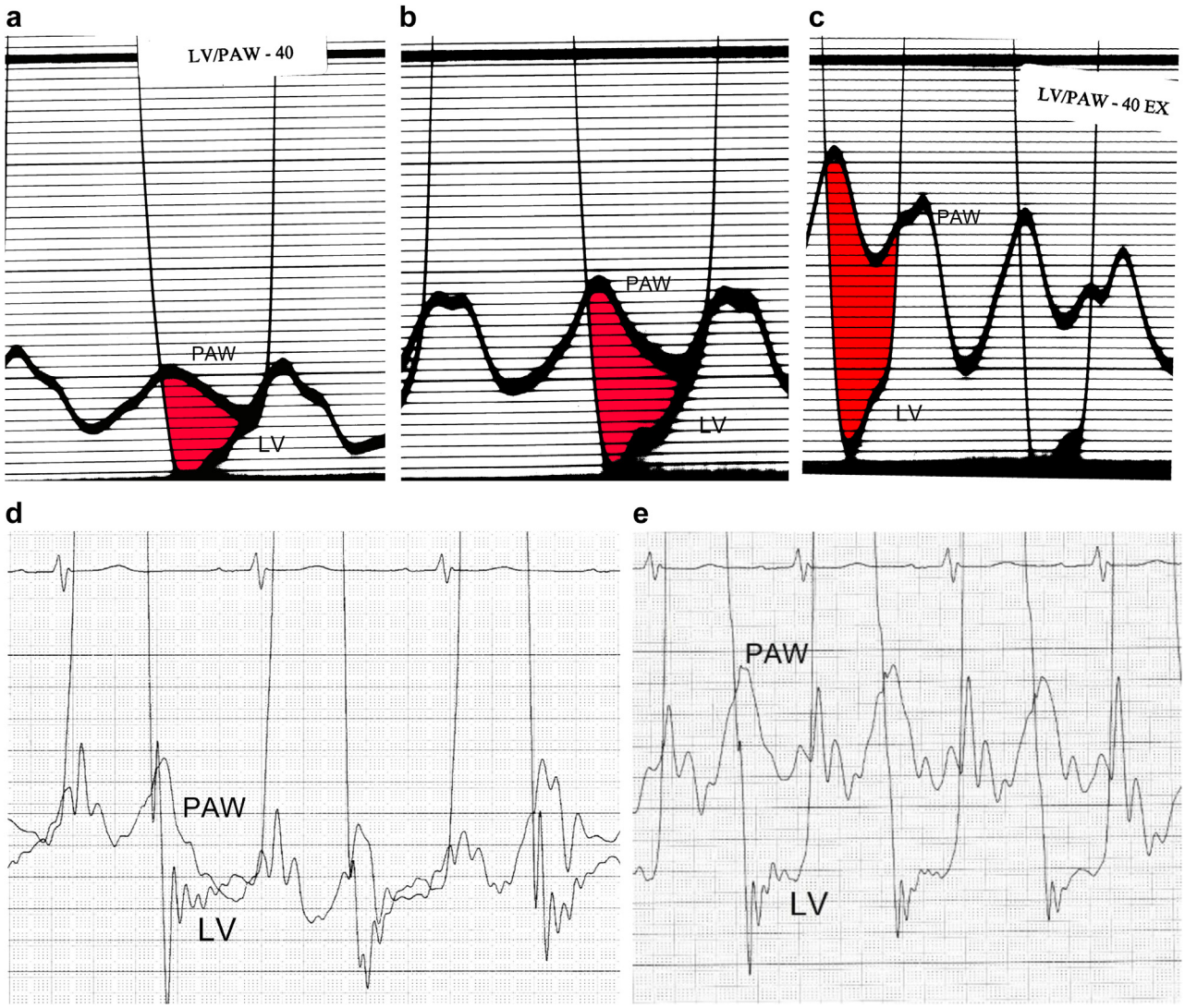

Figure 4. Hemodynamics (40 mm Hg scale) at rest (a and d) with responses to hydration (b), exercise (c), and dobutamine (e). In the first scenario, the patient had been NPO for 12 hours. Because of late-cycle diastasis albeit with doubling of the gradient after hydration (b) it was elected to exercise her on the table: note the dramatic response secondary to the typical increase in heart rate and transvalvular flow (c). In the last 2 panels, a similarly dehydrated and sedated patient with seemingly no gradient at rest (d) but known severe stenosis by echo was given dobutamine (e) with classic increase in gradient and markedly elevated end-diastolic left atrial pressure. Adapted from Turi ZG. Percutaneous Balloon Valvuloplasty. In *Hemodynamic Rounds: Interpretation of Cardiac Physiology from Pressure Waveform Analysis 4th Edition.* Kern MJ, Lim MJ, and Goldstein JA (editors). John Wiley 2018: pp 275-294.
Abbreviations: LV, left ventricle; PAW, pulmonary artery wedge pressure.

resistance, rather than just the right heart pressures alone, can be helpful in assessing the state of the pulmonary vascular bed. Occasionally, the gradient will appear low because of dehydration, in particular when the patient has been NPO for a prolonged period; in this setting, relatively small volumes of fluid can result in the demonstration of a substantial gradient (Figure 4a and b). Exercise on the cath table can be diagnostic (Figure 4c), but if a patient cannot exercise, dobutamine infusion can provoke a substantial rise in gradient when there is fixed valve obstruction (Figure 4d and e). The primary caution in cath lab hemodynamic assessment of MS is the overestimation of the gradient seen when left atrial pressure is estimated by pulmonary wedge pressure. This is particularly a concern in patients with mixed MS and MR, where the wedge-derived V wave amplitude is damped but contributes artifactually to the gradient because of the phase delay plus slow fall-off recorded across the pulmonary vascular bed throughout most of diastole (Figure 5). In addition, cath lab–derived mitral valve areas using the Gorlin formula are particularly prone to error if oxygen consumption is not measured (most labs use an estimate that may be off by 50% or more).

Screening—Stages of MS

The threshold for severe MS (Table 1) has changed with the multiple versions of the valve disease guidelines; 1.0 cm^2 was considered severe, but based on clinical course and symptomatology, this was revised to the 1.5 cm^2 threshold, whereas 1.0 cm^2 and below was considered "very severe."[24] The transvalvular gradient in isolation, given the confounding factors that influence it, is no longer included in the criteria for severity. However, it should be noted that pressure half-time remains a valuable adjunct, despite its dependence on compliance of the left atrium (LA) and LV, to distinguish the extent to which a high gradient is caused by stenosis rather than the multiple causes of high transvalvular flow highlighted earlier.

The "Progressive MS" category includes patients who have valve areas above the 1.5 cm^2 threshold. As discussed, these patients may merit intervention if they have exertional symptoms or exercise demonstrates features of hemodynamically significant MS and they have good valve anatomy[20]; however, the evidence base for intervention vs. medical therapy when heart rate slowing has not been attempted first is thin.

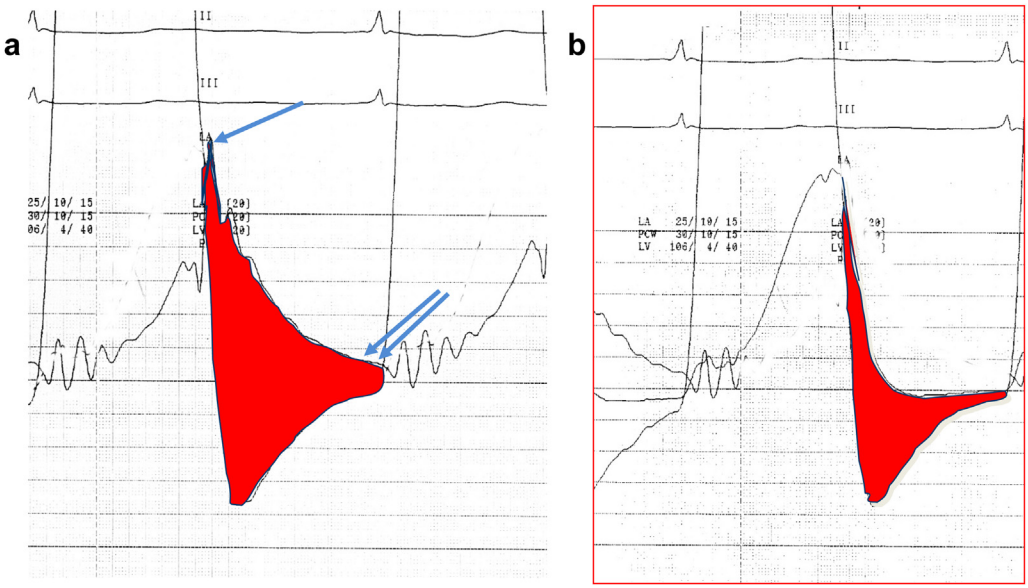

Figure 5. (a) Left ventricular and pulmonary wedge pressures (40 mm Hg scale) in a patient on the cath table at the beginning of a planned balloon mitral valvuloplasty. The gradient between the wedge and left ventricular pressure has been filled in red. Two features of this tracing make it uncertain that this is pure mitral stenosis: the height of the V wave (arrow) at rest is strongly suggestive of significant mitral regurgitation and the presence of diastasis at end diastole (double arrow) in the setting of a normal heart rate makes the severity of stenosis uncertain. (b) Transseptal puncture was performed, and left ventricular vs. left atrial pressure reveals the true nature of the patient's mitral valve pathology: the V wave remains high, consistent with mitral regurgitation, whereas near-diastasis is seen at mid-cycle, consistent with predominantly regurgitation rather than stenosis. The substantially higher gradient seen on the left reflects the delay in the peak V wave being shifted to the right and the much slower fall off in pressure (−dP/dt) occasioned by the transmission of left atrial pressure across the high-resistance pulmonary vascular bed. From Turi ZG. Percutaneous Balloon Valvuloplasty. In *Hemodynamic Rounds: Interpretation of Cardiac Physiology from Pressure Waveform Analysis 4th Edition.* Kern MJ, Lim MJ, and Goldstein JA (editors). John Wiley 2018: pp 275-294.
Abbreviations: LA, left atrium; LV, left ventricle.

Figure 3 shows the current American College of Cardiology/American Heart Association algorithm for screening for PBMV. In sum, for patients with ideal anatomy and symptomatic severe MS, PBMV is the procedure of choice (Class 1). This follows the randomized clinical trial evidence base, where balloon dilatation was first compared with closed surgical commissurotomy,[3,4] a procedure widely practiced in developing countries. Closed commissurotomy is a beating heart procedure and has advantages of not requiring a cardiac catheterization laboratory and using minimal disposables; thus, a cheap and reasonably effective alternative dating back some 70 years to the early surgical interventions for MS. Open commissurotomy, which requires heart lung bypass (and thus a membrane oxygenator among other disposables) has the benefit of commissurotomy under direct vision, but is substantially more expensive, frequently prohibitively so in countries where the disease is prevalent. In addition, relatively few active surgeons have experience with the technique, and in general, mitral valve replacement is usually the only surgical alternative available. PBMV appears to be noninferior or superior to both closed and open surgical techniques for patients with

Table 1
Stages of MS as shown in the American College of Cardiology/American Heart Association guidelines

Stage	Definition	Valve anatomy	Valve hemodynamics	Hemodynamic consequences	Symptoms
A	At risk of MS	Mild valve doming during diastole	Normal transmitral flow velocity	None	None
B	Progressive MS	• Rheumatic valve changes with commissural fusion and diastolic doming of the initial valve leaflets • Planimeteredmitral valve area >1.5 cm^2	• Increased transmitral flow velocities • Mitral valve area >1.5 cm^2 • Diastolic pressure half-time <150 ms	• Mild to moderate LA enlargement • Normal pulmonary pressure at rest	None
C	Asymptomatic severe MS	• Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets • Planimeteredmitral valve area ≤1.5 cm^2	• Mitral valve area ≤1.5 cm^2 • Diastolic pressure half-time ≥150 ms	• Severe LA enlargement • Elevated PASP >50 mm Hg	None
D	Symptomatic severe MS	• Rheumatic valve changes with commissural fusion and diastolic doming of the initial valve leaflets • Planimetered initial valve area ≤1.5 cm^2	• Mitral valve area ≤1.5 cm^2 • Diastolic pies-sure half-time ≥150 ms	• Severe LA enlargement • Elevated PASP >50 mm Hg	• Decreased exercise tolerance • Exertional dyspnea

LA, left atrium; MS, mitral stenosis; PASP, pulmonary artery systolic pressure.
Source: Otto CM, Nishimura RA, Bonow RO, et al. 2020 American College of Cardiology/American Heart Association guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2021; 77:e25-197

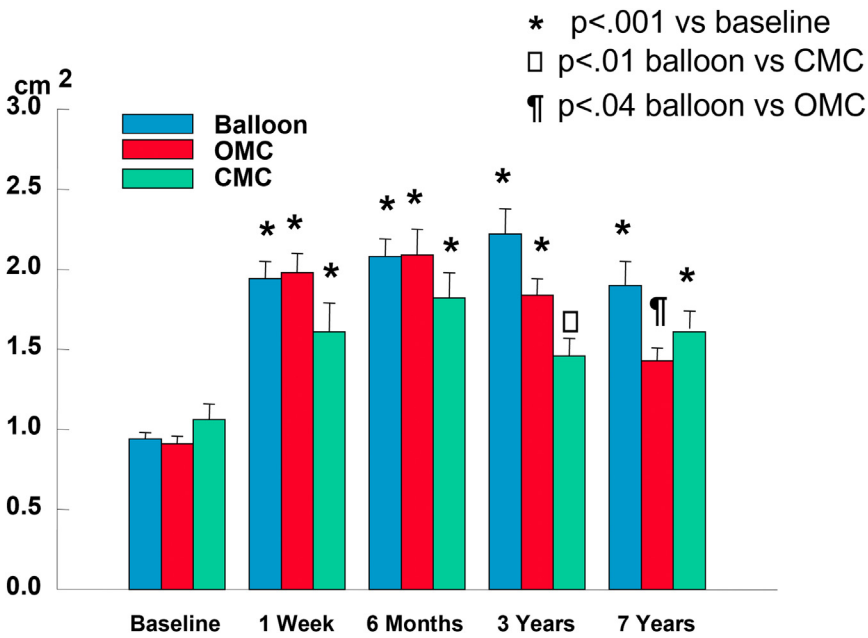

Figure 6. Mitral valve areas at baseline, 6 months, 3 years, and 7 years in patients randomized to balloon mitral valvuloplasty (n = 51), closed mitral commissurotomy (CMC; n = 19), and open mitral commissurotomy (OMC; n = 30). The data combine the results of 2 randomized trials.[4,5] The results of balloon dilatation were equal or superior to both surgical types in a population with ideal valve anatomy.

ideal valve anatomy (Figure 6).[5,6] For patients with less than optimal anatomy who are good surgical candidates, MV surgery is preferred; in contrast, for poor surgical candidates PBMV is the theoretical procedure of choice with the understanding that the results are inferior to those seen with ideal anatomy.[18]

Medication as First-Line Therapy

The sine qua non of medical therapy for MS is heart rate slowing and anticoagulation where indicated.[23] Keeping the resting heart rate slow and preventing a significant chronotropic rise with exercise can allow for substantial symptomatic improvement in sinus rhythm (Class 2a); however, patients with chronotropic incompetence may tolerate aggressive heart rate slowing poorly. On the other hand, failing to control heart rate results in substantially greater symptoms for any degree of MS. Atrial fibrillation is a particularly bad actor in MS because combination of loss of the atrial kick and the typical fast heart rate in untreated patients can precipitate acute pulmonary edema in a previously asymptomatic patient. Cardioversion can dramatically improve functional status and should be considered based on how long the patient has been in atrial fibrillation (AF) and the size of the left atrium. There has been a randomized trial comparing rate vs. rhythm control post-PBMV[25]; the latter resulted in substantially fewer symptoms, better 6-minute walk testing and quality of life as well as improvement in left atrial size. We have been influenced in selection of these patients by the experience of surgeons who routinely shock patients coming off bypass after mitral valve surgery; success rates for achieving and/or maintaining sinus rhythm decrease substantially with left atrial size $\geq$4.5 cm and in our experience is rare with left atrial size $\geq$6 cm. Cardioversion before ballooning or surgery is less likely to succeed because the underlying hemodynamic stress affecting the conduction system has not been addressed[23]; the exception may be patients who have had no previous effective heart rate slowing and are placed on optimal beta-blockade or its alternatives. The American College of Cardiology/American Heart Association and European Society of Cardiology guidelines recommend diuretics, beta-blockers, digoxin, calcium channel blockers that slow the heart rate and ivabradine as potential therapy for heart failure and heart rate slowing.[23,26] After cardioversion, amiodarone may be of benefit in some patients to maintain sinus rhythm as well as control heart rate; long-term tolerance is frequently an issue. Ablation has been attempted in a select population without clear evidence of long-term benefit.[27]

As for anticoagulation, the guidelines recommend vitamin K antagonists for patients with MS and atrial fibrillation, prior embolus, or LA thrombus; most practitioners will anticoagulate patients with spontaneous echo contrast in the LA or left atria >5.0 cm as well. The use of direct oral anticoagulants (DOACs) in MS remains without an evidence base and is generally considered contraindicated, although the concept is appealing; the maintenance of therapeutic range with vitamin K antagonists is difficult under any circumstances, but in developing countries monitoring of International Normalized Ratios represents a daunting obstacle (as do the cost of DOACs). A review from a national database in the Republic of Korea found thromboembolic events in a large population with MS treated with DOACs off label were significantly lower than those treated with warfarin.[28] There is an ongoing randomized trial (INVICTUS-ASA) comparing rivaroxaban to aspirin in RHD patients who cannot take vitamin K antagonists. Anticoagulation for MS patients in sinus rhythm without the risk factors cited lacks an evidence base. The benefits if any of antiplatelet agents alone in rheumatic MS is unknown. For patients with concomitant or recent coronary intervention, where oral anticoagulation is otherwise indicated, the consensus is for the use of oral anticoagulation plus a single antiplatelet agent after the initial peri-percutaneous coronary intervention period when dual antiplatelet therapy is otherwise typically given.[29]

Intervention

The algorithm for intervention (Figure 3) has evolved substantially and is currently focused on 2 pathways for patients with severe MS: those with symptoms and those without symptoms who warrant intervention because of the hemodynamic and electrophysiologic consequences of untreated MS. Care must be taken not to have sufficient delay that irreversible pulmonary vasculature or right heart changes occur or increase in left atrial size results in permanent AF. Thus, asymptomatic patients with severe MS and PHT (PA systolic >50 mm Hg) and those with new-onset AF have Class 2a and 2b indications, respectively.[23] Patients with

Table 2
How percutaneous balloon mitral valvuloplasty (PBMV) techniques have evolved

1. Preprocedure assessment—increasing use of commissural anatomy, 3D echo to determine suitability and for balloon sizing
2. Multiple revised scoring systems; Wilkins-Weyman echo score[17] remains standard
3. Access: many sites now use ultrasound guidance in keeping with the general shift in large vessel access in structural heart disease procedures
4. Sheath use: originally considered undesirable because of potential damage to the Inoue balloon, this is now considered ideal, typically 14F (which makes removing the deflated balloon somewhat difficult) or 16F
5. Anticoagulation—once restricted to heparin given after transseptal puncture; this has transitioned to partial anticoagulation after venous access and full anticoagulation after successful transseptal puncture; some sites routinely do PBMV under full anticoagulation throughout
6. Transseptal puncture—transitioned from exclusively fluoroscopy (still the case in some developing countries) to intracardiac echo (ICE) or transesophageal echo (TEE) guidance. With increasing ability to accurately locate area of puncture in the fossa ovalis, mid-mid to inferior-posterior is favored by most operators
7. TEE remains the primary imaging guidance overall, although improved ICE technologies and hybrid computed tomography, cath, noninvasive imaging are also used
8. General anesthesia rather than deep sedation is typical for patients undergoing TEE guidance
9. Balloon sizing: still predominantly using the height formula alone, with increasing incorporation of 3D imaging and intracommissural measurements
10. Vascular closure: figure of 8 skin suture or Perclose using "preclose" technique

what was previously termed mild MS whose valve areas fall above the 1.5 cm^2 threshold are now Stage B (Progressive, see Table 1), but who have "hemodynamically significant" MS induced with exercise and have suitable valve anatomy are considered to have Class 2b indications for PBMV. The European Society of Cardiology also lists as Class 2a indications in asymptomatic patients the presence of high thromboembolic risk as well as PHT, need for non-cardiac surgery and desire for pregnancy.[26]

The guidelines no longer include a pathway for asymptomatic "very severe" MS (valve areas $\leq$1.0 cm^2); previously intervention on this group was characterized as a 2a indication.[24] Nevertheless, this is a group on whom the procedure is often performed, part of a trend toward early percutaneous intervention for a variety of valvular heart diseases. In the case of MS, there is the expectation that any increase in metabolic demand in these patients, such as infection, may lead to rapid hemodynamic decompensation. Similar considerations apply for a patient planning to become pregnant. Early intervention in asymptomatic patients with only moderate MS has been studied, albeit in a nonrandomized comparison, suggesting fewer events, lower mortality, and better overall event-free survival when early PBMV was performed.[30]

The guidelines as well as an expert consensus document[31] recommend that the procedure be performed only in Comprehensive Valve Centers, the requirements for which do include experience with PBMV. However, in many otherwise qualified institutions, specific experience with PBMV is often lacking or it is infrequently performed; the maneuvers required are substantially different than with other SHD interventions, and judgment based on experience with individual elements of the procedure is essential for a reasonably predictable result. Even preparing the device for use has its own substantial learning curve.

Contraindications

Contraindications have generally included the presence of thrombus in the LAA and more than mild MR. With regard to the former, there have been a number of reports as well as some series where PBMV was performed despite documented LAA thrombus.[32] Most operators defer intervention until a prolonged period of anticoagulation to allow for resolution of thrombus; in the author's opinion, the ability to keep hardware from entering the appendage, even by highly skilled operators, is imperfect and potentially exposes patients to unnecessary risk of stroke. More than mild MR has been considered a relative contraindication (although some operators will routinely do PBMV in patients with mild to moderate or moderate MR); it is important to note that a 1 grade increase in MR, even with ideal commissural splitting, is common and should be expected; hence, the risk of severe MR may be substantial. In addition, overall outcomes are worse in patients with greater than mild MR at baseline.[18] Relative contraindications not specified in the guidelines include unfavorable commissural fusion as discussed, including absence of fusion, which would suggest that ballooning, dependent almost entirely on splitting of the commissures, is unlikely to be effective.[33]

Percutaneous Approach

The evolution of techniques for PBMV over 40 years has included changes in preprocedure evaluation, vascular access, intraprocedural imaging guidance, anticoagulation and anesthesia, and vascular closure. These are summarized in Table 2.

A number of approaches to access the mitral valve remain in use, but antegrade across the interatrial septum is used in nearly 100% of cases around the world. This requires transseptal puncture, a technique that was used only episodically for congenital heart disease, diagnostic studies of hypertrophic obstructive cardiomyopathy, and the occasional PBMV until the introduction of left-sided ablation by electrophysiologists led to an exponential rise in procedure volume in the 1990s.[34] The technique has evolved substantially during the 40 years since PBMV was introduced; it was performed initially with fluoroscopic guidance only which is still the practice in parts of the world where MS is endemic. With image guidance by intracardiac echo or TEE, precise access to the appropriate portion of the fossa ovalis can usually be achieved; a central fossa approach is recommended with consideration of a somewhat inferior and posterior location. The latter results in easier orthogonal positioning across the mitral annulus, similar to that required for TEER. The puncture itself can be performed with solid tipped needles (to avoid tissue embolization) or shaped nitinol needle tipped wires or radiofrequency catheters; the latter, given the typically thickened septum associated with chronic MS, may have advantages over needle passage in terms of failure to cross or tamponade.[35]

PBMV is typically done with TEE guidance, which in turn favors the use of general anesthesia, although it is done in some institutions under deep sedation. In developing countries, TEE may not be used, and hemodynamics, TTE, or even auscultation alone are used for assessing intermediate and final results. Anticoagulation, previously reserved for the posttranseptal phase, is now routinely administered (by oral or parenteral anticoagulation) before crossing the septum, an approach learned from electrophysiologists who have shown it to be associated with substantially fewer complications.[36] Continuous careful management of anticoagulation, catheter flushing, and prevention of air embolization is essential.

The Inoue balloon technique remains the dominant procedure used around the world. This device has remained largely unchanged since its development 40 years ago. Its key features are a latex balloon sandwiched between nylon mesh layers made of a loose weave over the distal surface and a tighter weave over the proximal surface. The density of the weave defines the compliance of portions of the apparatus, with the loosely woven high compliance distal portion inflating first, followed by the lower compliance proximal portion. Figure 7 shows the balloon centered around the mitral valve. A noncompliant band placed across the center of the balloon results in its inflating only after the barbell shape has been created, thereby centering the balloon across the valve. Balloon sizing typically uses a formula based on the patient's height, but it correlates poorly with the actual mitral valve area. Both a minimum mitral annular diameter[33] and maximum intercommissural diameter have been proposed as alternatives.[14]

Inflation techniques vary, but a stepwise dilatation method, starting with a balloon size several millimeters smaller than the maximum calculated followed by incremental increases in size, is the most commonly used.[37] With this method, the severity of MS and development of any increase in MR are assessed after each inflation; increase in MR by one grade or achievement of a suitable reduction in gradient dictate a stopping point. Some increase in MR is nearly invariable and typically occurs at the level of the split commissures. Splitting (vs. stretching) of

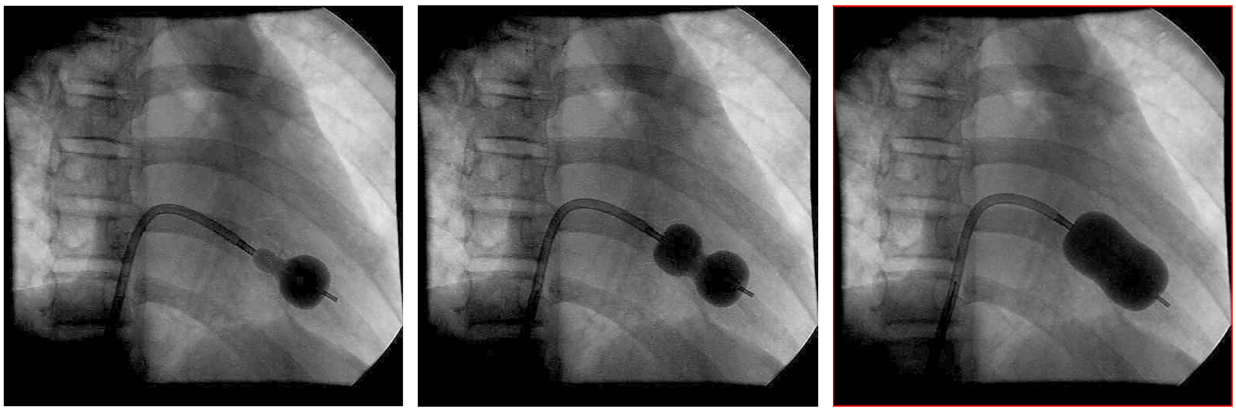

Figure 7. Sequential deployment of the Inoue balloon across the mitral valve. The image at left shows early inflation, with balloon expansion only of the distal portion in the left ventricle. The image in the center shows the balloon straddling the mitral valve just before final expansion (final frame) at the level of the waist of the balloon. Abrupt expansion on either side of the waist accompanies commissural splitting.

commissures can usually be appreciated by sudden expansion seen on fluoroscopy. It is better to accept some residual gradient than to persist with progressive inflations until severe MR occurs (Figure 8). An early flat rather than round appearance of the distal portion of the balloon is suggestive of severe subvalvular apparatus resistance or entrapment, and balloon inflation should be aborted. As the compliance curve of the balloon leads to an exponential rise in radial force in the final millimeter of inflation for any given balloon size (e.g., 27-28 mm in a 28 mm balloon), some operators avoid inflating in the final millimeter of a balloon's range to avoid additional risk of tearing the leaflets or subvalvular apparatus.[38] Generic versions of the balloon, with a single rather than dual inflation ports, are used in some parts of the world, albeit with a higher failure rate and risk profile in the experience of this author.

Attention is being paid to cerebral embolism in the periprocedure period for a number of structural heart interventions, in particular, TAVR. Thrombus, calcium, and tissue embolization have all been reported in the peri-PBMV period with an estimated stroke risk as high as 2.7%.[39] A small study by Freker et al[40] looked at carotid filter placement during TEER for MR and found debris in the filters of all 14 patients. The experience with cerebral protection in PBMV is limited to case reports,[41] but based on the data from these studies, there is significant likelihood that some of the low but significant stroke risk associated with the procedure may be addressable; however, a systematic study has not been performed. A case report involving aspiration "vacuuming" of the LAA to minimize embolic risk in PBMV has been reported in this journal.[42]

Postprocedure Management

Anticoagulation and rhythm management postprocedure, including cardioversion, is dependent on the indications already discussed. There is normally a 5 mm residual iatrogenic atrial septal defect induced by the 14F dilator and balloon passage across the septum. This normally resolves over the subsequent 6 months, with the proviso that there was sufficient improvement in the mitral valve area. In patients where the commissural splitting was inadequate and there is a residual gradient between the left and right atrium, it may perpetuate the fenestration and shunt. As immediate postprocedure hemodynamics can be influenced by residual left to right flow, leading to overestimation of the mitral valve area postprocedure, the final gradient and echo measurements should be recorded before withdrawing the sheath across the septum. Patients can typically be discharged within 24 hours; same-day discharge is feasible.[43]

Alternate Techniques

Alternative methodologies have included retrograde access, double balloon using cylindrical balloons, a monorail multiballoon system, single large cylindrical balloon, and a metal valvulotome. The latter was developed to allow for minimizing disposables, a luxury in developing countries. Unfortunately, it was even more technically challenging than standard PBMV and had the potential for lacerating the valve apparatus or the heart itself and is now obsolete.[44] Reuse of balloons, with multiple sterilizations, leads to loss of integrity of various components, occasionally with catastrophic failure[45]; a variety of clever adaptations to rescue these devices have been described in case reports. Parallel cylindrical balloons (the double balloon technique) placed across the mitral orifice are still used occasionally. The technique was introduced early in the PBMV experience, is cumbersome, has the somewhat increased risk of harpooning forward through the apex of the ventricle and has been largely abandoned. Alternatives to transfemoral venous access have included the antegrade transseptal approach via intrajugular and even transhepatic routes.

Outcomes

Immediate success rates have been excellent, well over 90% in most series, with typical valve area increases to the range of 2.0 cm^2. The standard definition of success has been an increase in valve area to $\geq$1.5 cm^2 and absence of severe MR; some have also included a reduction of the gradient by at least 50%. The outcomes have correlated with demographics, comorbidities, as well as physiological and anatomic features and have been extensively explored: the list includes age, prior valve intervention, AF, severity of baseline MR, PHT, and various echo scores and their individual components as already discussed.[14,18,21] Long-term outcomes correlate particularly strongly with initial results.

Improvements in valve area and hemodynamics, if initial results of PBMV are good, tend to persist in a young, ideal population. Nevertheless, our data show some loss of the gain is seen beyond 3 years (Figure 6). Five, 10 and 15-year event-free survival in a developing country population is in the range of 89%, 79%, and 43% respectively[46]; in contrast, data on older patients with less favorable valve anatomy in industrialized nations show substantially poorer long-term outcomes (56% event free at 10 years),[47] whereas 20-year event-free survival, although in follow-up restricted to patients with good initial results, was 30%.[48]

In addition to improved valve areas and gradients, PBMV has been associated with reduction in PHT and improved quality of life. Our data, albeit in relatively young patients with ideal valve anatomy, has shown near-complete reversibility of elevated pulmonary artery pressures and pulmonary vascular resistance regardless of how high the baseline values[49]; in older patients with chronic PHT, the data have been less convincing, likely because of irreversible changes in the pulmonary vasculature.[50] The LV dysfunction seen in some 30% of MS patients is

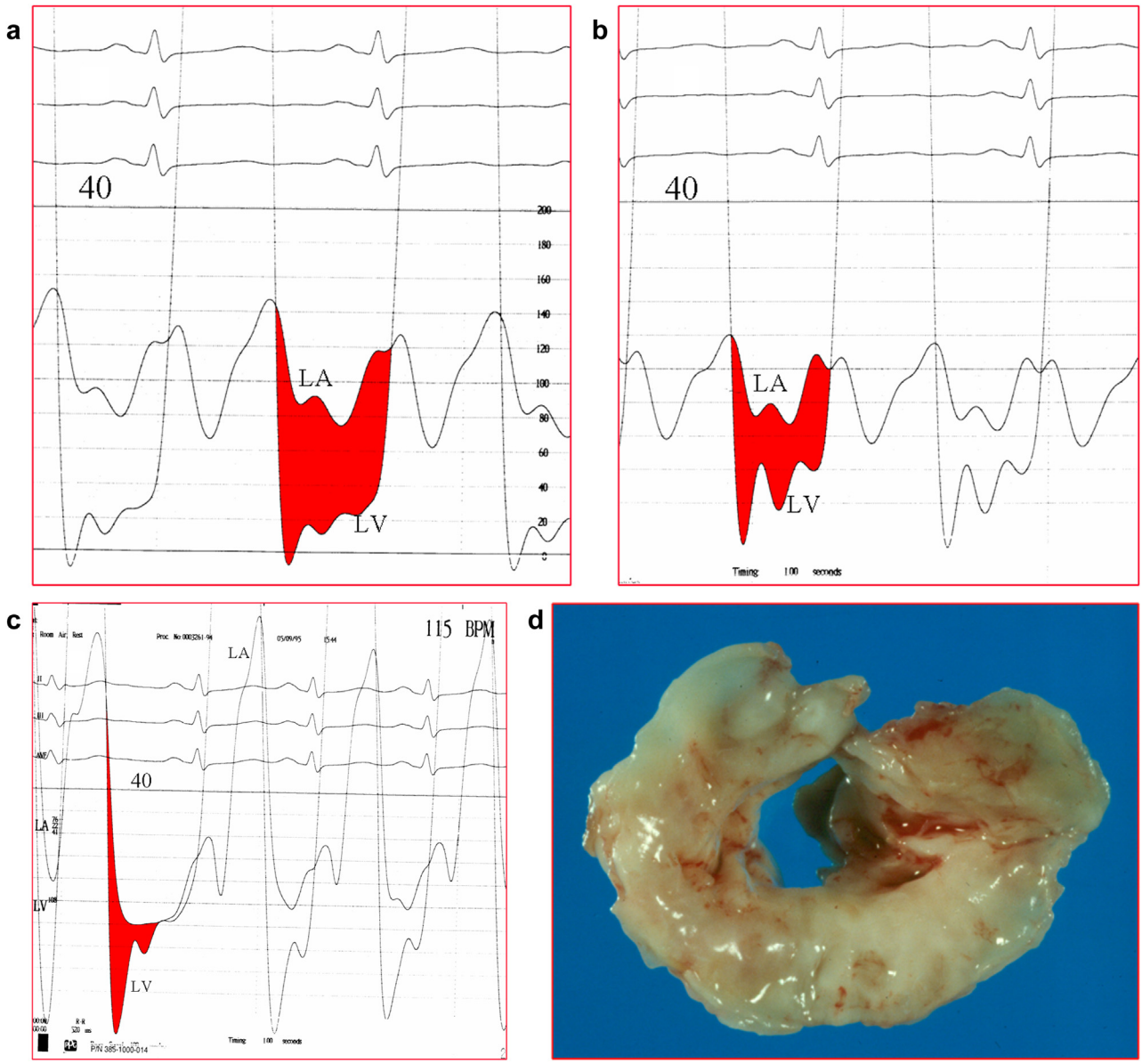

Figure 8. Balloon mitral valvuloplasty in a 32-year-old female with rheumatic mitral stenosis. Left ventricular (LV) vs. left atrial (LA) pressure (40 mm Hg scale) at baseline (a) and after the first inflation (b) reveal an approximately 50% reduction in gradient. Upsizing the balloon by an additional millimeter resulted in abolition of the gradient (C) but with a giant V wave consistent with severe mitral regurgitation. The patient was likely predisposed to the leaflet tear by heterogeneous thickening (d). She underwent successful mechanical mitral valve replacement. From Turi ZG. Percutaneous Balloon Valvuloplasty. In *Hemodynamic Rounds: Interpretation of Cardiac Physiology from Pressure Waveform Analysis 4th Edition.* Kern MJ, Lim MJ, and Goldstein JA (editors). John Wiley 2018: pp 275-294.

likely secondary to altered hemodynamic load rather than primary myocardial involvement from RHD[51]; although inconsistent, there is some evidence of left ventricular remodeling after successful PBMV, with improved global and regional LV function.[52]

Reviews of trends in the United States[53] as well as in Europe[54] over the past several decades correlate with a continuing decline in patients undergoing PBMV. In addition, there has been a strong trend toward the procedure being performed in older patients with less favorable anatomy and greater comorbidities with attendant less favorable results and substantially higher complication rates[53,54]; this may reflect waning of experience by operators as well as the greater inherent risk in these patients.

Complications

Complication of PBMV includes tamponade, severe MR, stroke, and death. The complication rate correlates strongly with operator experience[7] and has improved substantially with advances in imaging, in particular, tamponade secondary to errant transseptal puncture. The latter has benefited from the advent of echo-guided transseptal puncture whether by intracardiac echo or TEE; however, tamponade can result subsequently from manipulation of hardware in the LA and LV as well.[55] The rate of tamponade associated with PBMV, once in the range of 4%, has declined but remains a significant risk.[56] Air embolization is a potentially catastrophic complication and largely related to technique in handling of catheters and sheaths placed in the left atrium; typical manifestations are ST elevation, usually from right coronary embolism and occasional stroke. Thromboembolic stroke and myocardial infarction are typically related to failing to maintain adequate anticoagulation during the procedure, but calcium emboli have been reported, including a catastrophic saddle embolus in the left main.[57]

Severe MR, despite extensive efforts to predict risk, continues to occur in a significant portion of patients and is substantially dependent on

underlying anatomy as already discussed as well as operator decisions during the procedure. The reported rate is widely variable and likely dependent on the quality of MR assessment, but a careful study of 342 patients in the past decade revealed an 11.9% rate of moderate and 6.7% rate of severe MR induced by ballooning.[22] The impact of post-PBMV MR on event-free survival is dependent on the type and extent of MR, with leaflet tear at the central scallop or subvalvular disruption having early correlation with (frequently emergent) mitral valve replacement and cardiac death while commissural regurgitation is to be expected and tends to improve over time as the commissures refuse.[22] Figure 8 shows an example of catastrophic MR in a patient with seemingly good anatomy but likely uneven tissue characteristics that led to differential force exerted on portions of the valve leaflet with resultant leaflet tear.

Restenosis

Restenosis, like outcomes overall, correlates with age and anatomy; time to restenosis correlates with the initial improvement in valve area. Restenosis is typically defined as valve area <1.5 cm^2 and $\geq$50% loss of the initial gain. In a study from Saudi Arabia, patients with a mean age of 31 years had freedom from restenosis in 85%, 70%, and 44% at 5, 10, and 15 years, respectively.[46] The approach to restenotic MS, whether after prior surgical commissurotomy or PBMV, is largely dependent on the anatomy at the time that reintervention is being considered.[58] The success of reintervention largely correlates with elements of the echo scores, and in particular, with whether or not the commissures have refused and look amenable to splitting. If the commissures have not refused but the valve is hemodynamically restenosed, the likelihood that PBMV will be beneficial is low.[59] Although the results have typically been somewhat less impressive than dilatation of previously uninstrumented valves, this is likely because restenosis has been secondary to additional scarring and calcification. There is also increasing evidence of ongoing inflammation in patients with chronic rheumatic heart disease as manifested by elevated serum inflammatory markers[60] as well as findings of Aschoff bodies and inflammatory infiltration during histological examination of the left atrium.[61] This in turn may contribute to persistent atrial fibrillation and restenosis after PBMV. Overall, the literature is equivocal on whether PBMV or surgery has superior outcomes in patients with restenosis[62,63]; in general, event-free survival is lower with the former, driven by higher need for reintervention, but in the setting of favorable valve anatomy, PBMV remains reasonable as the procedure of choice.

Special Considerations

Multivalve Intervention

Concomitant valve disease, whether aortic or tricuspid, has special implications. In the case of mixed mitral and aortic valve disease, the typical scenario is MS with aortic insufficiency. In terms of clinical decision-making, much depends on whether or not the ventricle is already volume loaded from aortic regurgitation. If so, the "uncorking" of the left atrium by PBMV and especially the possibility of additional volume loading due to the typical increase in MR by at least 1 grade needs careful consideration. The threshold for intervening on both the aortic and mitral valve (whether percutaneous, surgical, or a combination) in the setting of a volume-loaded ventricle should be low; if instead, PBMV alone is performed, the patient needs to be monitored aggressively for signs of volume loading and dysfunction. If the combined mitral and aortic valve disease is MS and AS, then typically the AS should be addressed first or concomitantly, since relieving the MS alone will volume load the ventricle, which still has outflow obstruction. An uncommon scenario, mixed mitral and tricuspid stenosis, is an exception to relieving the forward obstruction first; PBMV before ballooning of the tricuspid valve will facilitate right to left shunting across the iatrogenically fenestrated intra-atrial septum if the left atrial pressure falls below the elevated right atrial pressure; hence, the tricuspid should be dilated first.[64]

Pregnancy

Pregnancy increases intravascular volume by as much as 50% along with an increase in heart rate; these in turn result in significant increase in transmitral gradient with potential for hemodynamic decompensation, in particular during later stages of gestation and the maximum stress of labor. The risks are related to the severity of MS, although even mild MS is associated with significant risk of heart failure.[65] Maternal and fetal mortality is increased, including miscarriage and stillbirths; maternal mortality has been reported as high as 34% in sub-Saharan Africa.[66] The presence of PHT, common in MS, in particular with concomitant lung disease or mixed MVD may be particularly morbid. One-quarter of pregnant patients with MS require hospitalization, and nearly half of those with severe MS because of heart failure.[65] Medical therapy to slow the heart rate and treat congestive heart failure typically includes beta-blockers, diuretics, and angiotensin-converting enzyme inhibitors and may be helpful, as may anticoagulation albeit with attention paid to teratogenicity of many of the potential regimens. The timing of PBMV is influenced by some plateauing of hemodynamic stress by 24 weeks and decreased theoretical risk from radiation as well as better fetal survival early in the third trimester.[67] In the absence of comparative studies, it should still be noted that maternal and fetal mortality appears to be higher with mitral valve surgery (both $\geq$20%).[68] Fetal monitoring during PBMV is essential; radiation should be minimized with proper shielding of mother and fetus, and some operators have done the procedure entirely with echo guidance. The overall results of PBMV in this setting have been good, but maternal and fetal risk remain.[69] Pre-pregnancy PBMV is preferred, including for patients with asymptomatic severe MS[23,26] because severe symptoms and decompensation during gestation are frequent. PBMV during pregnancy (Class 2a) should be restricted to symptomatic patients with moderate to severe MS and favorable anatomy or those with signs of hemodynamic stress because urgent or emergent mitral valve replacement has very high risk of fetal and potentially maternal mortality.[23] Caesarian section has not been shown to be of clear benefit, although it is commonly performed electively in MS patients.[70] Postdelivery heart failure has been well described.[65]

Mitral Annular Calcification and Bioprosthetic MS

Patients with calcified valves and subvalvular apparatus by definition will have high echo scores, and as discussed, less favorable short- and long-term results.[21,71] Mitral obstruction due to mitral annular calcification (MAC) is relatively common, particularly in elderly patients with multiple comorbidities, in particular, atherosclerotic disease, renal failure, hypertension, and concomitant valvular heart disease; because of comorbidities, these patients typically have poorer long-term outcomes than those with MS due to RHD, with $<$50% 5-year survival.[72] The potential physiological consequences are similar, with pressure overload of the left atrium associated with progressive increase in pulmonary venous pressures, PHT, and atrial fibrillation. In most cases, the obstruction is at the level of the annulus extending into the base of the valve leaflets and rarely involves the commissures. As such, balloon dilation is of little to no benefit; in our limited experience, patients undergoing PBMV where the primary pathology is MAC will have at most minimal short-term and typically no long-term benefit but will be at serious risk of periprocedural complications, including stroke and MR. A percutaneous approach with ballooning only is thus typically not considered although lithotripsy-assisted PBMV has been described, including with cerebral embolic protection.[73,74] Surgery in this setting has a significant complication rate with increased perioperative and long-term mortality[72,75] as well as less favorable outcomes and is recommended only when patients are highly symptomatic and medical therapy has failed.[23]

Valve-in-MAC placement of bioprosthetic valves designed for TAVR has a growing evidence base[76]; the procedure was initially plagued with an exceptionally high complication rate, including left ventricular outflow tract obstruction in particular, but also annular rupture, paravalvular leak, and valve embolization among others. The most recent data demonstrate the benefits of careful preprocedure planning, superior imaging, a number of techniques designed to prevent left ventricular outflow tract obstruction, and growing experience. Transcatheter mitral valve replacement for MAC with prostheses designed to be deployed in the mitral position is under investigation.[77]

PBMV alone for bioprosthetic stenosis has been performed with anecdotal reports of hemodynamic and symptom imporvement.[78] However, bioprosthetic stenosis is typically caused by leaflet fibrosis, and calcification and commissural fusion is rare.[79] Thus, the deployment of a balloon is likely to provide stretching and calcification fracturing rather than any long-term anatomic benefit. There is risk of embolization of thrombus, pannus, or calcium as well as MR due to leaflet disruption.

In contrast to valve-in-MAC, percutaneous valve-in-valve placement of TAVR valves has an excellent track record with a high success rate (near 100%), good short- and intermediate-term survival and relatively low complication rate in experienced hands, and is a Class 2a indication for patients who are at enhanced surgical risk.[23] The transmitral gradient does tend to be higher (7 vs. 5 mm Hg) than with surgical valve replacement, perhaps due to some degree of prosthesis-patient mismatch.[80] In practice, these patients tend to be at enhanced surgical risk, and thus, valve-in-valve is often performed as the procedure of first choice. Overall, additional details of valve-in-MAC and valve-in-valve, as well as valve-in-prosthetic ring procedures (for which PBMV alone has not been reported) have been reviewed in this journal[81,82] and are beyond the scope of our article.

Conclusions

PBMV is a highly effective and safe first choice for classic rheumatic MS with ideal anatomic features. It remains a viable alternative for some patients with less favorable anatomy who are also poor surgical candidates. It should be performed by operators with training and experience with PBMV working in Comprehensive Valve Centers. Although the procedure and technology have remained largely unchanged over 40 years, preprocedure imaging, image guidance, and periprocedure management have improved considerably. PBMV is declining in frequency in industrialized nations where the procedure has become relatively uncommon at the same time as the patients increasingly have less favorably anatomy and greater comorbidities with attendant increase in complication rates. However, it remains an important therapeutic tool, particularly in parts of the world where rheumatic heart disease is endemic.

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