Percutaneous Approaches to Valvular Disease
Alec Vahanian, MD; Igor F. Palacios, MD

Until the early 1980s, surgery was the only possible treatment for severe valvular lesions; then, a new alternative appeared: percutaneous balloon valvuloplasty.

We deal here with percutaneous valvuloplasty for acquired valvular stenoses and also briefly describe the first steps of percutaneous valve replacement and repair.

Percutaneous Mitral Commissurotomy
Rheumatic mitral stenosis continues to be endemic in developing countries, where mitral stenosis is the most frequent valve disease. Although the prevalence of rheumatic fever has greatly decreased in Western countries, it continues to represent an important clinical entity because of outmigration from developing countries. The figure given by the registry Euro Heart Survey, run in 2001, shows that mitral stenosis accounts for 12% of the single native valve disease.

K. Inoue and colleagues were the first to perform percutaneous mitral commissurotomy (PMC) in 1982. The good results obtained by the technique have led to its increasing worldwide use.

Evaluation Before PMC
Clinical evaluation is the first step of the decision to intervene. Under particular scrutiny here are functional disability and any possible risks with surgery. The assessment of anatomy aims to eliminate contraindications and define prognostic considerations. The presence of left atrial thrombosis is the main contraindication for the technique and requires the performance of transesophageal echocardiography before the procedure. Echocardiographic assessment allows the classification of patients into anatomic groups with a view to predicting the results. Most authors use the Wilkins score (Table 1), although others use a more general assessment of valve anatomy (Table 2). More recently, scores have been developed that take into account the uneven distribution of anatomic abnormalities, in particular in commissural areas. In fact, none of the scores available have been shown to be superior to the others.

Technique
The transvenous approach is the most widely used. Transseptal catheterization is the first step of the procedure and one of the most crucial. The transarterial approach could represent an alternative in the rare cases in which the transseptal approach is contraindicated or impossible. There are currently 2 main techniques: balloon commissurotomy and metallic commissurotomy.

In balloon commissurotomy, the 2 major techniques are the double-balloon technique and the Inoue technique.

The double-balloon technique is effective but demanding and carries the risk of left ventricular perforation by the guidewires or the tip of the balloons. The multi-track system is a recent variant of the double-balloon technique and aims to make the procedure easier through the use of a monorail balloon and only a single guidewire.

The Inoue technique has become the most popular worldwide. The design of the Inoue balloon allows safe and fast positioning across the valve. In addition, it is pressure extensible, allowing for the performance of a stepwise dilation (Figure 1). The available data comparing the Inoue technique and the double-balloon technique suggest that the Inoue technique makes the procedure easier; that both have equivalent efficacy, although the double-balloon technique may result in a slightly larger valve area; that the long-term results are equivalent; and that the Inoue balloon carries a lower risk because the risk of left ventricular perforation is virtually avoided.

Cribier et al introduced the metallic commissurotomy, which uses a device similar to the Tubbs dilator used during closed surgical commissurotomy (Figure 2). The experience reported with this device includes more than 1000 patients, primarily from developing countries. These initial results suggest that its efficacy is similar to that of balloon commissurotomy, but the risk of hemopericardium seems higher. In addition, this technique is more demanding for the operator than the Inoue technique. The potential advantage of metallic commissurotomy is that the dilator is reusable, which reduces the cost of the procedure. A definitive comparison of the respective merits of the 2 methods requires further data on metallic commissurotomy and adequate randomized comparisons.

Results
The technique has now been evaluated in several thousand patients with different clinical situations. The results of PMC can be assessed in the catheterization laboratory using hemodynamics or echocardiography. Although echocardiography may be difficult to perform in the catheterization laboratory

From the Cardiology Department, Bichat Hospital, AP-HP, Paris, France (A.V.), and the Cardiac Unit, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Mass (I.F.P.).
Correspondence to Alec Vahanian, MD, Cardiology Department, Bichat Hospital, 46, rue Henri Huchard, 75018 Paris, France. E-mail alec.vahanian@bch.ap-hop-paris.fr
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The failure rates range from 1% to 15%, and they reflect primarily the learning curve of the operators. Procedural mortality ranges from 0% to 3%. The incidence of hemopericardium varies from 0.5% to 2%. Embolism is encountered in 0.5% to 5% of cases. Severe mitral regurgitation is the most worrying complication. It occurs in 2% to 10% of patients and results from noncommissural leaflet tearing, primarily in cases with unfavorable anatomy, and even more so if there is a heterogeneous distribution of the morphological abnormalities. Surgery is often necessary later and can be conservative in cases with less severe valve deformity.

Although urgent surgery is seldom needed for complications (<1% in experienced centers), it may be required for massive hemopericardium or, less frequently, for severe mitral regurgitation, leading to hemodynamic collapse or refractory pulmonary edema. Immediately after PMC, color Doppler echo shows small intratral shunts in 40% to 80% of cases.

**Predictors of Immediate Results**

The prediction of the immediate results is multifactorial. In addition to morphological factors, preoperative variables (such as age, history of commissurotomy, functional class, small initial mitral valve area, and presence of tricuspid regurgitation) and procedural factors (such as the nonuse of Inoue technique) are independent predictors of poor immediate results.5,17

**Long-Term Results**

We are now able to analyze follow-up data up to 15 years. Several large single-center series confirm the late efficacy of PMC in a large population comprising a variety of patient subsets (Table 3). Late outcome after PMC differs according to the quality of the immediate results.

When the immediate results are unsatisfactory, patients experience only transient or no functional improvement. The prognosis for patients with severe mitral regurgitation is usually poor, and surgical treatment is usually required in the months after PMC. In cases of insufficient initial opening, delayed surgery is usually performed when the clinical conditions allow it. However, in some patients, moderate improvement in valve function provides functional improvement for several years, although they must be carefully followed up to allow for a timely operation.

Conversely, if PMC is initially successful, survival rates are good; the need for subsequent surgery is infrequent, and functional improvement occurs in the majority of cases.
When functional deterioration occurs in these patients, it is later and related primarily to mitral restenosis. The incidence of restenosis, as assessed by sequential echocardiography, is approximately 40% after 7 years. Repeat PMC can be proposed if recurrent stenosis leads to symptoms. At the moment, we have only a small number of series available on repeat PMC; they show encouraging results in selected patients with favorable characteristics when restenosis occurs several years after an initially successful procedure and if the predominant mechanism of restenosis is commissural refusion. Finally, repeat PMC is the sole option in patients with contraindications for surgery.

Follow-up studies have shown that the degree of mitral regurgitation remains on the whole stable or decreases slightly during follow-up. Atrial septal defects are likely to close later in the majority of cases. Successful PMC decreases the intensity of spontaneous left atrial contrast, reduces the size of the left atrium, and improves left atrial function. Even if these findings do not constitute proof of the efficacy of PMC on thromboembolism or even more so on atrial fibrillation, they consistently show the beneficial effect of the procedure on the causes of these conditions.

**Predictors of Long-Term Results**

Prediction of the long-term results is also multifactorial and is based on clinical variables (such as age), valve anatomy, factors related to the evolutionary stage of the disease (eg, functional class), atrial fibrillation, history of previous commissurotomy, severe tricuspid regurgitation, cardiomegaly, and high pulmonary pressure. Finally, it is closely related to the quality of the immediate results, as assessed by final gradient, valve area, and degree of regurgitation.

**Selection of the Candidates**

The first step is to eliminate a contraindication; then, it is necessary to evaluate the individual risk-benefit ratio, taking into account clinical and anatomic variables and finally the local conditions in terms of availability and expertise in the interventional procedure and surgery.

Contraindications to PMC are summarized in Table 4. It has been suggested that PMC be performed in patients with moderate stenosis in the hope of delaying the natural course of the disease. However, these patients are usually candidates for medical treatment, and the risks of PMC outweigh the benefits. The most important contraindication is the presence of left atrial thrombosis. A contraindication is self-evident if the thrombus is floating or localized in the cavity or on the interatrial septum. However, no consensus has been reached in cases with thrombosis localized in the left atrial appendage. In our opinion, in such cases, the indications for PMC should be limited to patients with contraindications to surgery or surgical candidate.

**Figure 1.** Inoue balloon technique. Progressive inflation of Inoue balloon across mitral valve. Right anterior oblique 30°.

**Figure 2.** Metallic commissurotomy. A, Metallic commissurotome is positioned across the mitral valve in closed position; B, metallic commissurotome is opened. Right anterior oblique 30°. Adapted with permission from Cribier et al.
those without urgent need for intervention when oral anticoagulation can be given for at least 1 month before PMC and a new transeophageal echocardiographic examination shows the disappearance of the thrombus.

Severe tricuspid regurgitation is not a contraindication for the procedure; however, surgery is preferable if it is associated with severe organic tricuspid valve lesions resulting in refractory heart failure.

Finally, if excluding left atrial thrombosis, the true contraindications for transseptal catheterization are rare in practice: severe scoliosis, obstruction of the inferior vena cava, and major abnormalities of the interatrial septum.

Indications

PMC is the procedure of choice when surgery is contraindicated or very high risk or for patients with favorable characteristics, ie, young patients with favorable anatomy. In this latter population, we have available several randomized studies comparing PMC and surgical commissurotomy. They show that PMC is at least comparable to surgical commissurotomy with regard to immediate and long-term results. In addition, if restenosis occurs, these patients could undergo repeat PMC or surgery without the difficulties and inherent risks resulting from pericardial adhesion and chest wall scarring.

Conversely, much remains to be done in refining indications for the other patients, especially those with few or no symptoms and those with unfavorable anatomy.

Because of the small but definite risk inherent in the technique, truly asymptomatic patients are not usually candidates for the procedure, except in the following cases: (1) when there is increased risk of thromboembolism (eg, previous history of embolism, dense spontaneous contrast in the left atrium, recurrent atrial fibrillation); (2) when there is a risk of hemodynamic decompensation (severe pulmonary hypertension [systolic pulmonary pressure >50 mm Hg at rest or >60 mm Hg during exercise]); (3) when there is the need for extra-cardiac surgery; or (4) when the patient is or is considering becoming pregnant. In this respect, exercise testing, including exercise echocardiography whenever possible, is useful in patients claiming to be asymptomatic if it is not consistent with the other findings. In such patients, PMC should be performed only by interventionists with considerable experience in the technique and if valve anatomy is favorable, in which case a safe and successful procedure can be expected.

Patients with unfavorable anatomy are common in Western countries. Unfortunately, no randomized study is available for these patients, and a comparison of the results of PMC with those of surgical series is difficult because of the differences in the patients and surgical techniques involved. In practice, when surgery is performed in these patients, it is valve replacement, with the inherent risk during the postoperative period and, even more importantly, the long-term morbidity related to prosthetic complications.

For this group of patients, some favor immediate surgery because of the less satisfying results of PMC, whereas others

<table>
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<th>TABLE 4. Contraindications for Percutaneous Mitral Commissurotomy</th>
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<td>Mild mitral stenosis (valve area &gt;1.5 cm)</td>
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<td>Left atrial thrombosis</td>
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<tr>
<td>Mitral regurgitation &gt;2/4</td>
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<tr>
<td>Massive or bicommissural calcification</td>
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<td>Need for open-heart surgery on another valve, or coronary arteries, or ascending aorta</td>
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<tr>
<td>Contraindications for transseptal catheterization</td>
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Figure 3. Echocardiographic monitoring during stepwise Inoue balloon technique. Progressive opening of anterior commissure with an increase in valve area from 1.2 to 2 cm². Two-dimensional echocardiography. Short-axis view. Courtesy of Dr E. Brochet.
prefer PMC as an initial treatment for selected patients, resorting to surgery in the event of failure and/or secondary deterioration. In such cases, the decision must be individualized, and one should take into account the multifactorial nature of the prediction of the results for patient selection. Available data suggest that continuing good long-term results may be obtained and PMC may be useful to defer surgery in selected patients—for example, those with mild to moderate calcification or severe impairment of the subvalvular apparatus but with otherwise favorable characteristics, such as young or middle age, or sinus rhythm (Figure 4). Conversely, valve replacement should be performed in patients with severe calcification, particularly if the other characteristics are also unfavorable.

Such a strategy, starting with PMC and performing surgery secondarily in case of need, can also be proposed when the risk of surgery is high: in the elderly, in whom PMC can be considered as a palliative treatment; in patients with a previous history of surgical commissurotomy or aortic valve replacement; and during pregnancy if symptoms persist despite medical therapy.

The complication rate of the procedure is clearly related to the experience of the team. There are no available guidelines for the performance of PMC. However, PMC probably should be restricted to groups whose experience of transseptal catheterization has been positive and who have successfully carried out an adequate number of procedures on a regular basis, thus improving their technical performance and ability to select patients. This recommendation carries even more weight in Western countries, where mitral stenosis is infrequent.

**Percutaneous Aortic Valvuloplasty**

Severe degenerative calcified aortic stenosis is the most frequent valve disease in Western countries, accounting for the initial interest in its potential treatment by interventional cardiology. The percutaneous aortic valvuloplasty (PAV) technique was described by Cribier et al in 1985.

**Technique**

The femoral approach is the most frequently used. The alternative is the antegrade approach, which necessitates a transseptal catheterization and results in a difficult procedure. Valvuloplasty is performed with balloons from 20 to 25 mm in diameter.

The results of PAV can be assessed during the procedure by use of measurements of valve area by hemodynamics. However, the value of these measurements is highly questionable because of the hemodynamic instability of the patients and the very early loss in valve area after the procedure. The most viable method for assessing the results is measuring the valve area by echo Doppler in the days after the procedure.

**Results**

As could be expected from the anatomic lesions in severe degenerative aortic stenosis, ie, absence of commissural fusion and extensive calcification, PAV has only a limited efficacy. Overall, it reduces tight stenosis to moderate stenosis with a final valve area between 0.7 and 1.1 cm². This is clearly inferior to the valve area obtained with a valvular prosthesis, which usually provides a valve area >1.5 cm².
Risks
Mortality and morbidity of the procedure are high. Hospital mortality varies from 3.5% to 13.5%, and within 24 hours, 20% to 25% of the patients have at least 1 serious complication, in particular vascular complications at the puncture site.36

Long-Term Results
Despite a relatively modest improvement in valve function, it is common to note a degree of functional improvement of short duration. However, the benefit decreases and finally disappears after a few months.38,39 An aortic valve replacement has been performed subsequently with good results in selected patients, but the prognosis for the others is particularly poor.39 Overall, it is now recognized that PAV alone does not change the natural course of the disease. The poor midterm results are primarily due to the clinical status of the patients and the moderate and transient improvement in valve function obtained by PAV.

Selection of the Patients
No randomized comparisons are available between PAV and surgery. Therefore, the indications should take into account the excellent results of aortic valve replacement, when it is possible, and the poor results of PAV.

Most groups have abandoned the technique,2 whereas for others, it would appear that there is a very limited role in critically ill patients with cardiogenic shock and multivisceral failure.24 A few reports suggest that good midterm results can be obtained if secondary operation is possible.40 However, this 2-step approach should be compared with immediate surgery to establish its efficacy. This technique also had a limited role in (1) in patients who must undergo emergency non-cardiac surgery, (2) in palliation in cases with absolute or non–life-threatening short-term contraindications to surgery when a significant disability exists, or (3) in patients who refuse surgery.

Other Percutaneous Valve Dilatation
Other applications of percutaneous valve dilatation are used very sparingly. The few procedures performed show that these interventions are feasible, but they are insufficient in number to allow us to evaluate results and establish indications. At the present time, it seems that indications for percutaneous tricuspid valvuloplasty are rare and reserved for patients presenting a tight tricuspid stenosis, either pure or associated with mild regurgitation.41

Percutaneous dilatation of bioprostheses may give rise to severe immediate complications at the level of the left heart and give poor midterm results in the tricuspid position.42

Percutaneous Valve Replacement and Repair
Today, the surgical approach is the only option available for valve replacement, which is performed in several hundred thousand patients each year. Despite the proven efficacy of surgical valve replacement, it still carries a high operative mortality and morbidity in the growing population of patients at high risk because of their cardiac and/or extracardiac conditions. This sets the stage for the emergence of less invasive techniques.

The first experiments on percutaneous catheter-based valve replacement started in the mid-1960s.43–47 The era of percutaneous valve replacement in humans started with the report by Bonhoeffer et al48,49 in 2000 on percutaneous pulmonary valve replacement.

This was a real stimulation for moving to percutaneous implantation of an aortic valve. Here again, experimental work was performed by Bonhoeffer et al using a bovine jugular vein containing a valve that was dissected and sutured into a stent.50 Initially, the valve was implanted in the descending aorta, mimicking the Hufnagel approach used for aortic valve replacement in the 1950s.51 Then the valve was implanted in an orthotopic position.52 Lutter et al53 performed similar experiments with a porcine aortic valve mounted into a self-expandable nitinol stent. These experiments showed that implantations in the subcoronary aortic position was technically difficult in the animal model because of problems with positioning, early migration, and risk of damage to the coronary circulation or to the mitral valve because of the very short distance between the coronary ostia and the mitral valve. The orientation mechanism described by Bonhoeffer et al52 was a step forward in preventing the risk of coronary occlusion. Finally, in vitro testing54,55 showed a satisfactory durability of the devices for a period up to 2 years.

The latest step in this new era was the first percutaneous aortic valve implantation in humans, performed by Cribier, in late 2002, in a 57-year-old man with severe aortic stenosis, cardiogenic shock, and contraindications for surgery.54 An antegrade approach was used, and the valve was successfully implanted within the native aortic valve with stable positioning and no coronary artery flow obstruction (Figure 5). Valve function was good, because aortic valve area was 1.6 cm², with only a mild aortic regurgitation. However, the patient died of severe extracardiac complications 4 months later despite continuing good valve function. Since then, 6 other such procedures have been performed in compassionate indications (Alain Cribier, MD, personal communication, 2003).

In the field of percutaneous mitral valve repair, we are at an even earlier stage. Preliminary experimental studies used different devices, either mitral rings introduced via the coronary sinus or stitches mimicking the Alfieri operation. In addition, the first implantations in humans, both permanent and temporary, have been performed very recently but have not yet been published (Ted Feldman, MD, personal communication, 2003).

Future
Pragmatically, a larger use of PMC will depend on the solution of economic problems that limit the use of the technique in the countries in which rheumatic disease is still endemic but in which means are lacking. In the industrialized countries, the debate on the use of PMC in patients with unfavorable anatomy will require further studies including a large number of patients and a long follow-up. Further proofs of the efficacy of PMC in the prevention of embolism and atrial fibrillation are necessary to further extend the indications to asymptomatic patients. New tools, such as 3D echocardiography,56 may help to refine patient selection and
better assess the results. Intracardiac echocardiography could avoid the need for transesophageal echocardiography to exclude left atrial thrombosis and help in transseptal puncture, the pitfall being the price of the device.57 Finally, in the future, it could be possible to perform PMC in combination with other percutaneous procedures, such as durable coronary revascularization (with the availability of drug-eluting stents), ablation in patients with supraventricular arrhythmias, or occlusion of the left atrial appendage to prevent stroke.

The question with regard to the ring annuloplasty are that the coronary myopathies with low ejection fraction. These 2 groups of severe mitral regurgitation of ischemic origin or in cardio-myopathies with low ejection fraction. What will be the ideal material? Jugular bovine veins are limited in size, and their outcome in the systemic circulation is unknown. Valves made of polymer or biological material, collapsible and compressible, are to be designed and evaluated to show biocompatibility and low profile. Should we prefer balloon- or pressure-expandable stents? The latter may decrease the risk of periprosthetic leakage in a calcified annulus but could have insufficient radial force in cases of calcified stenotic valves.

With regard to percutaneous valve repair, there is a field for potential clinical applications in patients with moderate to severe mitral regurgitation of ischemic origin or in cardio-myopathies with low ejection fraction. These 2 groups of patients are at high risk for surgery and, in practice, are often treated with only a ring annuloplasty. The potential pitfalls with regard to the ring annuloplasty are that the coronary sinus is not located exactly at the level of mitral annulus but rather is intra-atrial. The “edge-to-edge” technique is expected to be very technically demanding. In addition, experience from surgery showed us that residual mitral regurgitation is often noted after either isolated annuloplasty or edge-to-edge repair alone. This leads us to expect that a combination of techniques will be necessary. Thus, the early enthusiasm of the interventionists, together with a climate of heightened commercial activity, should not make us lose sight of the fact that these devices should be evaluated experimentally to test their feasibility and durability; then, a careful clinical assessment should be performed.58,59 Finally, lessons from the past suggest that in this field, a close collaboration between interventionists and surgeons is of utmost importance.

Conclusions

After more than 15 years of extensive clinical evaluation, the technique of percutaneous valvuloplasty, which for practical purposes can be summed up as PMC, has a significant place in the treatment of mitral stenosis. Finally, the first applications of percutaneous aortic valve replacement in humans opens a new era for research and potential clinical application for the percutaneous treatment of acquired valve disease.

References


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