Late Results of Percutaneous Mitral Commissurotomy in a Series of 1024 Patients

Analysis of Late Clinical Deterioration: Frequency, Anatomic Findings, and Predictive Factors

Bernard Iung, MD; Eric Garbarz, MD; Pierre Michaud, MD; Steeven Helou, MD; Bruno Farah, MD; Patricia Berdah, MD; Pierre-Louis Michel, MD; Bertrand Cormier, MD; Alec Vahanian, MD

Background—The optimal use of percutaneous mitral commissurotomy (PMC) in a wide range of patients requires accurate evaluation of late results and identification of their predictors.

Methods and Results—Late results of PMC were assessed in 1024 patients whose mean age was 49±14 years. Echocardiography showed that 141 patients (14%) had pliable valves and mild subvalvular disease, 569 (55%) had extensive subvalvular disease, and 314 (31%) had calcified valves. A single balloon was used in 26 patients, a double balloon in 390, and the Inoue Balloon in 608. Good immediate results were defined as valve area $\geq 1.5 \text{ cm}^2$ without regurgitation $\geq 2/4$ (Sellers’ grade) and were obtained in 912 patients. Median duration of follow-up was 49 months. The 10-year actuarial rate of good functional results (survival with no cardiovascular death and no need for surgery or repeat dilatation and in New York Heart Association [NYHA] class I or II) was 56±4% in the entire population. Follow-up echocardiography was available in 90% of the patients who experienced poor functional results after good immediate results and showed restenosis in 97% of these. In multivariate analysis, the predictors of poor functional results were old age ($P=0.0008$), unfavorable valve anatomy ($P=0.003$), high NYHA class ($P<0.0001$), atrial fibrillation ($P<0.0001$), low valve area after PMC ($P=0.001$), high gradient after PMC ($P<0.0001$), and grade 2 mitral regurgitation after PMC ($P=0.04$).

Conclusions—PMC can be performed with good late results in a variety of patient subsets. Prediction of late events is multifactorial. Knowledge of these predictors can improve patient selection and follow-up. (Circulation. 1999;99:3272-3278.)

Key Words: mitral valve $\bullet$ balloon $\bullet$ valvuloplasty $\bullet$ follow-up studies

The safety and immediate efficacy of percutaneous mitral commissurotomy (PMC) have been widely demonstrated for $>10$ years. However, the consequences of its widespread use are less well known, because large published series report mainly midterm follow-up, do not always include a great diversity of patient subsets, and do not report anatomic findings associated with late deterioration.

We report herein on the longest follow-up after PMC in a large single-center series, in which clinical events are detailed according to the quality of the immediate results. In the patients who had good immediate results from PMC, we analyzed the frequency of late clinical deterioration, associated anatomic findings, and predictive factors.

Methods

Study Population

From March 1986 to March 1995, 1024 consecutively admitted patients residing in France underwent PMC in our department. Their characteristics are described in Table 1; 5.6% had left ventricular ejection fraction $<0.45$. The usual contraindications to the procedure were previously detailed.

Technique

All procedures were performed via the antegrade transvenous approach. We used a single balloon in 26 cases and a double balloon in the 390 subsequent cases. After October 1990, the Inoue balloon was systematically used in 608 patients, according to the stepwise technique, under echocardiographic guidance.

Measurements

Echocardiography was performed in the same laboratory on the day preceding PMC and 24 to 48 hours afterward.

Mitrail valve anatomy based on transthoracic echocardiography and fluoroscopy has been classified in 3 groups, as previously detailed: flexible valves and mild subvalvular disease (chordae $\geq 10$ mm long) (group 1), flexible valves and extensive subvalvular disease (chordae $<10$ mm long) (group 2), and calcified valves confirmed by fluoroscopy (group 3). In a subset of 40 patients, the mean±SD (range) Wilkins score was 8.0±0.8 (7 to 9) for echocardiographic, fluoroscopic, and operative views.
TABLE 1. Baseline Characteristics of the 1024 Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>49±14</td>
</tr>
<tr>
<td>Female sex</td>
<td>848 (83)</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>5 (1)</td>
</tr>
<tr>
<td>II</td>
<td>232 (22)</td>
</tr>
<tr>
<td>III</td>
<td>745 (73)</td>
</tr>
<tr>
<td>IV</td>
<td>42 (4)</td>
</tr>
<tr>
<td>Previous commissurotomy</td>
<td>163 (16)</td>
</tr>
<tr>
<td>Previous embolism</td>
<td>119 (12)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>408 (40)</td>
</tr>
<tr>
<td>Cardiothoracic index</td>
<td>0.51±0.06</td>
</tr>
<tr>
<td>Valve anatomy</td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>141 (14)</td>
</tr>
<tr>
<td>Group 2</td>
<td>569 (55)</td>
</tr>
<tr>
<td>Group 3</td>
<td>314 (31)</td>
</tr>
<tr>
<td>Left atrial diameter, mm (time-motion echocardiography)</td>
<td>50±8</td>
</tr>
<tr>
<td>Valve area (echocardiography), cm²</td>
<td>1.1±0.2</td>
</tr>
<tr>
<td>Mean gradient (Doppler), mm Hg</td>
<td>10±4</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>641</td>
</tr>
<tr>
<td>1</td>
<td>373</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
</tr>
</tbody>
</table>

Values are mean±SD or n (%).

Follow-Up
Clinical follow-up was performed at 1-year intervals since 1986. It was based on visits to the department or on a standardized questionnaire sent to the patient’s cardiologist. Any unexplained death was considered cardiovascular related.

Follow-up was concluded in June 1997, and patients were considered lost to follow-up if their last contact was before June 1996. Follow-up was completed for 994 patients (97%), and the median duration was 49 months (range, 1 to 132 months).

End Points
Good immediate results were defined by a composite end point that associated a mitral valve area ≥1.5 cm² with no regurgitation ≥2/4.

Clinical events occurring during follow-up were combined in the following end points: (1) global survival; (2) survival considering only cardiovascular-related death, noncardiovascular death being censored at the time of death; (3) survival considering no cardiovascular-related death or need for mitral surgery or repeat dilatation; and (4) “good functional results,” ie, survival considering no cardiovascular-related death or need for mitral surgery or repeat dilatation and patient in New York Heart Association (NYHA) functional class I or II. Survival status was censored at the time of surgery or repeat dilatation.

Statistical Analysis
Cumulative survival curves were determined for these 4 end points of late results according to the Kaplan-Meier method. Continuous variables and actuarial survival rates were expressed as mean±SD, except for follow-up duration, which was expressed as a median. In the predictive analysis, continuous variables were divided into subgroups with clinically chosen cutoff points. Comparisons before and after PMC were made by use of paired Student’s t test.

The aim of the predictive analysis was to identify the predictors of late clinical deterioration after good immediate results from PMC (valve area ≥1.5 cm² with no regurgitation ≥2/4). Predictive analysis concerned the predefined end point of “good functional results.” Univariate analysis was performed with a Cox model that included 1 covariate and concerned the 12 preprocedure variables, the 2 procedure-related variables, and the 3 postprocedure variables listed in Table 2. Variables with P<0.25 were entered in a Cox multivariate model with a backward selection procedure and a significance level of P=0.25. Two-way interactions were studied between these selected variables with a stratified log-rank test. The final Cox multivariate model was established by a backward selection of these variables with a significance level of P=0.05.

A predictive model of continuing good functional results was established with the final Cox model, in which the baseline survival function So(t) was estimated from the study population. We validated this model by comparing the predicted and observed numbers of good and poor functional results at 7 years in the study population, according to the method described by Lemeshow and Hosmer. The quality of the discrimination achieved with the final Cox model was measured by the area under the receiver-operating characteristic (ROC) curve. Validation and testing of the model were performed at 7 years to ensure that late functional results were accurately estimated, because 211 patients had ≥7-year follow-up, 58 of whom experienced ≥1 cardiovascular event.

All data were entered prospectively in a computerized database beginning in 1986. Analysis was performed with SAS statistical software (SAS Institute Inc, release 6.11).

Results

Immediate Results
Severe adverse events were in-hospital death in 4 patients (0.4%), embolism with sequelae in 3 (0.3%), severe mitral regurgitation with Sellers’ grade ≥3 in 35 (3.4%), and vascular complications requiring surgery in 11 (1.1%). No tamponade occurred in this series.

After PMC, mean valve area increased from 1.1±0.3 cm² (P<0.0001), and mean gradient decreased from 10±4 to 5±2 mm Hg (P<0.0001). Mitral regurgitation was absent after the procedure in 318 patients and was recorded as grade 1 in 441 patients, grade 2 in 222, grade 3 in 32, and grade 4 in 3.

Good immediate results as defined by the composite end point were obtained in 912 patients (89%). The 112 poor immediate results were related to valve area <1.5 cm² in 77 cases and Sellers’ grade mitral regurgitation ≥3 in 35. All cases of death or embolism occurred in patients with poor immediate results.

Late Results
The cumulative curves of late events are represented in Figures 1, 2, 3, and 4.

In the entire population of 1024 patients, 10-year actuarial rates were 85±4% for global survival, 92±2% for survival considering only cardiovascular-related deaths, 61±4% for survival with no need for surgery or repeat dilatation, and 56±4% for good functional results.
The events that occurred during follow-up are detailed in Table 3. Thirty-seven deaths were cardiovascular in origin (heart failure in 24, sudden death in 6, stroke in 4, and myocardial infarction in 3). The other 25 deaths were caused by neoplasia in 13 patients, respiratory insufficiency in 6, suicide in 2, cirrhosis in 1, AIDS in 1, accident in 1, and Alzheimer disease in 1. A subsequent procedure was performed on the mitral valve in 183 patients, including 135 who had valve replacement. The procedures combined with mitral surgery were, singly or in combination, aortic valve replacement in 14, tricuspid annuloplasty in 5, and coronary bypass grafting in 3. The 46 patients who were in NYHA functional class III or IV were awaiting operation or were medically treated because of refusal to undergo surgery or contraindications to surgery.

Of the 112 patients who had poor immediate results, only $19 \pm 4\%$ were free from surgery, and $14 \pm 3\%$ had good functional results at 5 years (Figures 1 through 4). Surgery was performed in 74 patients. Median duration between
unsuccessful balloon commissurotomy and surgery was 1 month (range, 1 to 54 months). Surgery was conservative in 9 patients with severe mitral regurgitation and 5 with insufficient valve opening.

For the 912 patients who had good immediate results, 10-year actuarial rates were 87±4% for global survival, 93±2% for survival considering only cardiovascular-related deaths, 67±4% for survival with no need for surgery or repeat dilatation, and 61±5% for good functional results (Figures 1 through 4). After good immediate results, a new procedure on the mitral valve was performed in 109 patients, the median duration being 48 months (range, 1 to 115 months). Valve replacement was the most frequent treatment. Open-heart commissurotomy was performed in 13 patients and repeat dilatation in 21 with favorable anatomy. Follow-up echocardiography was available in 154 (90%) of the 172 patients who experienced poor functional results (cardiovascular death, surgery, repeat PMC, or symptoms in NYHA class III or IV). It showed a mean valve area of 1.2±0.2 cm² and mitral restenosis, as defined by a valve area <1.5 cm² and a loss >50% of the initial gain, in 150 patients (97%). Mitral restenosis was pure in 125 cases and combined with a regurgitation ≥2/4 in the remaining 25. In the patients who underwent surgery, surgical findings confirmed mitral restenosis as assessed by echocardiography. Of the 15 patients who had combined surgery, progression of aortic valve disease was the major reason for surgery in 5 cases.

Predictive Factors of Late Results
Univariate predictors of late results after a successful PMC are detailed in Table 2; neither of the procedure-related variables was predictive (type of balloon, \( P = 0.72 \); effective balloon dilating area, \( P = 0.92 \)).

Multivariate analysis identified 7 predictors of late functional results after good immediate results from PMC (Table 4). Four predictors were preprocedural characteristics, and the other 3 were related to the immediate results.

The good fit of the model was shown by the absence of significant difference between predicted and observed results at 7 years (\( \chi^2 = 5.3, \text{df}=5, P=0.38 \)). The area under the ROC curve was 0.71 (Figure 5).

Discussion
In this single-center series that reports clinical follow-up after PMC in 1024 patients, 10-year actuarial rates of survival with no cardiovascular-related death, no subsequent procedure on the mitral valve, and good functional results were 56±4% in

![Figure 2. Survival considering only cardiovascular-related deaths.](image)

![Figure 3. Survival considering cardiovascular-related deaths with no need for mitral surgery or repeat dilatation.](image)

![Figure 4. "Good functional results" (survival considering cardiovascular-related deaths with no need for mitral surgery or repeat dilatation and in NYHA functional class I or II).](image)
the entire population and 61 ± 5% after good immediate results. Mitral restenosis, pure or associated with regurgitation, was documented in most of the patients who had poor functional results after good immediate results from PMC. The occurrence of poor functional results was related to the baseline characteristics of the patients and to the quality of the immediate results.

### Late Clinical Deterioration After PMC

As has been shown with surgical commissurotomy, late outcome differs according to the quality of the immediate results. Inadequate correction of valve impairment leads to only transient or no functional improvement.18,19 On the other hand, good immediate results generally provide sustained improvement, and when functional deterioration occurs, it is late and mainly related to mitral restenosis.20 The present study clearly shows the same findings with regard to PMC.

Of our 112 patients who had poor immediate results, 94 (84%) experienced ≥1 cardiovascular event, and the majority underwent early mitral valve replacement. In such patients, the indication and timing of surgery depended on confounding factors such as comorbidities and the prevailing views of the medical and surgical teams. Our policy is to recommend early surgery after poor immediate results from PMC, without waiting for secondary deterioration. Patients who did not undergo surgery generally had contraindications to surgery, and most of them died of cardiovascular causes or became rapidly symptomatic.

Conversely, only 172 (19%) of the 912 patients with good immediate results experienced cardiovascular events. In the patients who experienced poor functional results, follow-up echocardiography showed mitral restenosis in 97% of cases. Valve replacement was frequently required because of unfavorable anatomy or mitral regurgitation greater than or equal to grade 2. Those who had isolated mitral restenosis with favorable anatomy underwent open-heart commissurotomy or a second dilatation.

### Predictive Factors of Late Clinical Deterioration

The predictive analysis of late functional results was based only on patients who had good immediate results to eliminate the consequences of poor immediate results. The high number of events reported in the present series and the diversity of the population enabled predictive factors to be analyzed accurately.

The values of the relative risks indicate that patients cannot be classified as at high risk for poor late results on the basis of a single predictor and that prediction of late results is multifactorial.

Age has been identified as a predictor of late results in series of surgical21,22 or balloon commissurotomy.6 As was the case after surgical commissurotomy,21 mitral valve anatomy was a predictor of midterm results in most series of balloon commissurotomy, whatever the scoring system used.23–25 The few studies including echocardiographic follow-up have shown that impaired valve anatomy increases the risk of restenosis.26,27 Two other predictors are related to the evolutive stage of the cardiopathy, ie, functional class and atrial fibrillation, which have been identified as predictors of late outcome in series of balloon4,6,7 and surgical commissurotomy procedures.21

The prognostic value of these 4 patient-related characteristics provides useful data to improve selection of candidates for PMC. Because late outcome depends strongly on the

### Table 4. Multivariate Analysis of Predictors and Relative Risks of Poor Late Functional Results in 912 Patients Who Had Good Immediate Results of PMC*

<table>
<thead>
<tr>
<th>Variable and Subgroups</th>
<th>Relative Risk (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>0.0008</td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>50–70</td>
<td>1.5 (1.2–2.0)</td>
<td></td>
</tr>
<tr>
<td>≥70</td>
<td>2.4 (1.4–3.9)</td>
<td></td>
</tr>
<tr>
<td>NYHA functional class</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>I–II</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>III–IV</td>
<td>2.7 (1.7–4.4)</td>
<td></td>
</tr>
<tr>
<td>Rhythm</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Sinus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2.0 (1.4–2.7)</td>
<td></td>
</tr>
<tr>
<td>Echocardiographic group</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.5 (1.1–1.9)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.2 (1.3–3.7)</td>
<td></td>
</tr>
<tr>
<td>After procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valve area, cm²</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>≥2.00</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1.75–2.00</td>
<td>1.4 (1.1–1.7)</td>
<td></td>
</tr>
<tr>
<td>1.50–1.75</td>
<td>1.9 (1.3–2.8)</td>
<td></td>
</tr>
<tr>
<td>Mean gradient, mm Hg</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>≤3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>3–6</td>
<td>2.0 (1.6–2.5)</td>
<td></td>
</tr>
<tr>
<td>≥6</td>
<td>4.0 (2.5–6.2)</td>
<td></td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>0 or 1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.4 (1.0–2.0)</td>
<td></td>
</tr>
</tbody>
</table>

*Valve area ≥1.5 cm² with no regurgitation >2/4.

![Figure 5. ROC curve obtained by testing the multivariate model. Area under the curve is 0.71.](http://circ.ahajournals.org/Downloaded from/Multivariate Analysis of Predictors and Relative Risks of Poor Late Functional Results in 912 Patients Who Had Good Immediate Results of PMC*)
presence of good immediate results, patient selection must also take into account factors that are only predictors of immediate results, such as initial valve area or previous commissurotomy.\textsuperscript{1–3}

In the present series, 3 predictors of late results were related to the quality of the immediate results. The prognostic value of final mitral valve area is well known,\textsuperscript{4–7,9} and it remained a strong predictor in patients who had a valve area $\geq 1.5$ cm$^2$ after PMC. Mean mitral gradient was the other strong predictor related to immediate results. It provided information that was additional to mitral valve area, which suggests the potential interest of an end point of good immediate results that combines valve area and gradient. The third predictor of late results in our series, although of less prognostic value, was the presence of moderate mitral regurgitation after PMC (Sellers’ grade 2).

These predictors are of particular relevance for follow-up. Patients who have good immediate results but who are at high risk for further events must be carefully followed up to allow for timely intervention.

The 2 procedure-related variables did not modify late outcome in the present study, which is the only series comprising a high number of patients who have undergone PMC with both of the most widely used techniques, ie, the double balloon and the Inoue balloon.

The test of the model shows that it is not possible to achieve perfect discrimination in the prediction of late outcome. This is not related to insufficient modeling, because the model fits to observed data, but to intrinsic limitations in the prediction of late outcome, as was also shown for immediate results.\textsuperscript{9}

**Late Results of PMC and Mitral Surgery**

Late results of series of PMC and mitral surgery must be analyzed with reference to patient characteristics. Randomized studies have shown that the results of closed- or open-heart commissurotomy were not better than those of PMC, but these studies were performed only in populations comprising a limited number of patients, all of whom were young.\textsuperscript{28,29}

No randomized study is available for older patients who have a less-favorable outcome,\textsuperscript{4,6–7} and a comparison with surgical series is difficult because of the differences in the patients involved and the fact that the surgical alternative can be not only commissurotomy but also valve replacement.

**Limitations of the Study**

The present study does not enable the rate of restenosis after PMC to be established accurately. This could be achieved only with repeat echocardiographic examinations, standardized in their technique and frequency regardless of patient symptoms. Echocardiographic follow-up was not prospectively planned in the present study because it would have been difficult to perform owing to the number and geographic diversity of the patients involved. Nevertheless, echocardiographic data were obtained in 90% of patients who had poor functional results after an initially successful PMC.

In our previous experience of follow-up after successful PMC, we found that hemodynamic variables did not provide any additional information to clinical and echocardiographic variables in a multivariate model.\textsuperscript{40} For this reason and to simplify the procedure, we have not performed systematic hemodynamic measurements before and after PMC since 1994. In the present series, we did not study the predictive value of hemodynamic variables to avoid a bias related to a high number of patients with missing data in our multivariate analysis. For the same reason, we did not mention atrial shunts after PMC. Generally, they are small and decrease or disappear on follow-up.\textsuperscript{31}

**Clinical Implications**

This single-center series confirms the late efficacy of PMC in a large population comprising a variety of patient subsets. The identification of the predictors of late outcome provides useful information in improving patient selection and follow-up.

Good continuing results can be expected in patients with favorable characteristics. When late clinical deterioration occurs, the high frequency of restenosis suggests the potential interest of repeating PMC.

Patients with nonideal anatomy are more frequently encountered in western countries and form a particularly heterogeneous group with regard to their other characteristics. Because prediction of late clinical deterioration is multifactorial, selection of these patients must not rely exclusively on valve anatomy but should take into account all other predictors. Furthermore, the strong predictive value of the quality of the immediate results stresses the importance of evaluating them carefully on the basis of valve area and gradient.

**References**


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