Reinterventions after percutaneous mitral commissurotomy during long-term follow-up, up to 20 years: the role of repeat percutaneous mitral commissurotomy

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Aims
We analysed reinterventions performed during long-term follow-up after percutaneous mitral commissurotomy (PMC) with a particular focus on freedom from mitral surgery and late results of repeat PMC.

Methods and results
In 912 patients who had good immediate results of PMC (valve area $\geq 1.5$ cm$^2$ with mitral regurgitation $\leq 2/4$), we analysed survival without reintervention (surgery or repeat PMC) and survival without surgery alone, with a follow-up up to 20 years. The median age was 48 years, and 251 patients (27%) had calcified valves. During a median follow-up of 12 years, 351 patients (38%) underwent a reintervention: surgery was performed in 266 (76%) patients and repeat PMC in 85 (24%). Cardiovascular survival without reintervention (surgery or repeat PMC) was $38 \pm 2\%$ at 20 years. When analysing cardiovascular survival without surgery, this rate increased to $46 \pm 2\%$ at 20 years. In the 504 patients aged $\geq 50$ years at the time of their initial PMC, 20-year rates were $45 \pm 3\%$ for cardiovascular survival without reintervention and $57 \pm 3\%$ for cardiovascular survival without surgery. Of the 85 patients who underwent repeat PMC, cardiovascular survival without surgery was $60 \pm 7\%$ at 10 years.

Conclusion
After successful PMC, reintervention is frequently needed. However, almost half of the patients remained free from surgery at 20 years. Repeat PMC was performed in one out of four cases of reintervention in this study, thereby allowing for postponement of surgery in a substantial number of patients.

Keywords
Mitral stenosis • Balloon commissurotomy • Mitral valve surgery

Introduction
Percutaneous mitral commissurotomy (PMC) is the reference treatment for mitral stenosis in patients with favourable valvular anatomy. Older patients with less favourable conditions are frequently encountered in Western countries and are also potential candidates for PMC. We recently reported 20-year outcome after PMC according to the composite endpoint of good functional results, identified its predictive factors, and proposed a score to estimate individual patient outcome. As in all other series of PMC, mitral surgery and repeat PMC were studied in this paper as a single endpoint of reintervention. After a successful PMC, late deterioration is generally due to mitral restenosis. When mitral surgery is needed for restenosis, it is often a mitral valve replacement, with the inherent operative mortality and long-term risk of prosthesis-related complications. Repeat PMC has also been shown to be feasible with good mid-term results in a limited number of series. Since the major goal of PMC is to postpone surgery as far as possible, the possibility to repeat this procedure to further defer mitral surgery is therefore a major
interest of the technique. However, the analysis of freedom from mitral surgery and results of repeat PMC during long-term follow-up have never been specifically studied.

We present here a detailed analysis of reinterventions performed in a series of 912 patients followed up to 20 years after successful PMC, with a specific focus on survival without surgery alone. In addition, we analysed the results of repeat PMC. We also tried to identify patients in whom repeat PMC is particularly useful to delay mitral surgery.

Methods

Patients

From March 1986 to March 1995, 1024 consecutively admitted patients residing in France underwent PMC in our department, 912 of whom (89%) had good immediate results, defined as mitral valve area ≥ 1.5 cm² and mitral regurgitation < 2/4.10,14,18,27,28 These 912 patients form the basis of the present study and their characteristics are detailed in Table 1. The median age was 48 years. Most patients were highly symptomatic in New York Heart Association (NYHA) class III or IV and 352 patients (39%) were in atrial fibrillation.

Technique

All the procedures were performed using the antegrade transvenous approach. A single balloon was used in the first 17 patients, then a double balloon was used in 338 patients. Finally, beginning in October 1990, we used the Inoue balloon in the remaining 557 patients, according to the stepwise technique under echocardiographic monitoring. Repeat PMC was considered in symptomatic patients with mitral restenosis due to bicommissural fusion with no mitral regurgitation > 2/4.21 All of the repeat PMCs were performed using the Inoue balloon.

Measurements

Echocardiographic examinations were performed by experienced operators in the same laboratory on the day preceding PMC and 24–48 h after the procedure. The reference measurement for valve area was planimetry by two-dimensional echocardiography. When planimetry was not feasible, the Doppler pressure half-time method was used instead.27 The degree of mitral regurgitation was assessed

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline characteristics of the whole population and according to patient age at the time of their initial percutaneous mitral commissurotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole population (n = 912)</td>
<td>&lt;50 years (n = 504)</td>
</tr>
<tr>
<td>Age, year</td>
<td>Median [IQR] or n(%)</td>
</tr>
<tr>
<td>Female, sex</td>
<td>755 (83)</td>
</tr>
<tr>
<td>NYHA functional class</td>
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</tr>
<tr>
<td>I–II</td>
<td>223 (25)</td>
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<tr>
<td>III</td>
<td>657 (72)</td>
</tr>
<tr>
<td>IV</td>
<td>32 (3)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>352 (39)</td>
</tr>
<tr>
<td>Previous commissurotomy</td>
<td>135 (15)</td>
</tr>
<tr>
<td>Valve anatomy (Cormier’s score)</td>
<td></td>
</tr>
<tr>
<td>Class 1</td>
<td>136 (15)</td>
</tr>
<tr>
<td>Class 2</td>
<td>525 (58)</td>
</tr>
<tr>
<td>Class 3</td>
<td>251 (27)</td>
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<tr>
<td>Extent of valve calcification</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>661 (72)</td>
</tr>
<tr>
<td>1</td>
<td>153 (17)</td>
</tr>
<tr>
<td>2</td>
<td>63 (7)</td>
</tr>
<tr>
<td>3–4</td>
<td>35 (4)</td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>50 [45–54]</td>
</tr>
<tr>
<td>Valve area (echocardiography), cm²</td>
<td>1.1 [0.9–1.2]</td>
</tr>
<tr>
<td>Mean gradient (Doppler), mmHg</td>
<td>10 [7–12]</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>612 (67)</td>
</tr>
<tr>
<td>1</td>
<td>290 (32)</td>
</tr>
<tr>
<td>2</td>
<td>10 (1)</td>
</tr>
</tbody>
</table>

IQR, interquartile range.
before and after PMC according to Sellers’ classification on left ventriculography in a 30° right anterior oblique view. In cases of missing data, we used an assessment by colour Doppler.29

Valve anatomy was classified into three groups, according to Cormier’s score: flexible valves and mild subvalvular disease (chordae ≥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).30,31 The extent of valve calcification was quantitated into four grades using fluoroscopy according to a previously described classification.32

Follow-up

Follow-up took into account the 912 patients residing in France who underwent successful PMC. Data were collected either during patient’s visits to the department or by a standardized questionnaire sent to the patient’s cardiologist. In case of missing data, an interview was performed by telephone with the patient or his/her cardiologist or general practitioner. Follow-up was concluded in December 2008. Patients were considered lost to follow-up if their last contact was before January 2008.

The events taken into account for the follow-up were: death (from cardiovascular or non-cardiovascular origin), mitral surgery or repeat PMC. These events were combined in the following endpoints: (i) overall survival; (ii) cardiovascular survival; (iii) cardiovascular survival without reintervention (either mitral surgery or repeat PMC); (iv) cardiovascular survival without mitral surgery alone. Survival status was censored at the time of surgery.

Statistical analysis

All data were entered prospectively in a computerized database starting from 1986.

Continuous variables were expressed as median and interquartile range (25th–75th percentiles). Comparisons between subgroups used the Mann–Whitney U test for continuous variables and the chi-square test for qualitative variables. Comparisons before and after PMC used the paired Wilcoxon test. Cumulative survival curves were determined by the Kaplan–Meier method.

We analysed the factors associated with cardiovascular death or mitral surgery. Univariable analysis used a Cox proportional hazards model for 14 variables: 11 pre-procedure variables listed in Table 1, the type of balloon and effective balloon dilating area, and three post-PMC variables (valve area, mean gradient, and mitral regurgitation). Variables with P ≤ 0.20 were entered in a multivariable Cox proportional hazards model with a backward selection procedure and a significance level of P = 0.05.

To assess the relationship between the age group and the risk of reintervention, we used a Cox univariable model to study hazard ratios between age in decades and cardiovascular survival without surgery.

Analysis was performed with SAS statistical software (SAS Institute Inc. SAS Institute, Cary, NC, USA).

Late results

Follow-up was completed for 814 patients (89%) with a median follow-up period of 144 months (interquartile range 54–189). The 98 patients lost to follow-up in 2008 were analysed for their available median follow-up of 62 months (interquartile range 34–84). The comparison between patients with complete follow-up and those lost to follow-up is shown in Supplementary material online, Table S1.

Death occurred in 136 patients and was from cardiovascular cause in 79 (58%) of them.

The most frequent events were interventions on the mitral valve in 351 patients. A repeat PMC was performed in 85 patients (24%) while 266 patients (76%) were surgically managed. Isolated mitral valve surgery was performed in the majority of cases (208 patients, 78% of all surgical procedures) and was mitral valve replacement in 189 patients and valve repair in 19. Of the 58 patients (22%) who underwent combined surgery, the associated procedure was aortic valve replacement in 52 patients and coronary artery bypass grafting in 6 patients.

At 20 years, overall survival was 75 ± 2% and cardiovascular survival was 85 ± 2%. Twenty-year rates were 38 ± 2% for cardiovascular survival without reintervention (either surgery or repeat PMC) and 46 ± 2% for cardiovascular survival without mitral surgery (Figure 1).

Risk of surgery and age groups

The relationship between age in decades and cardiovascular survival without surgery is depicted in Figure 2. It shows a significant increase in the risk of surgery after the age of 50.

Results

Immediate results

The 912 consecutive patients with good immediate results of PMC (i.e. final mitral valve area ≥1.5 cm² and mitral regurgitation <2/4) did not experience any major adverse event defined as in-hospital death, tamponade, or embolism leaving sequelae. After PMC, the median valve area increased from 1.1 to 1.9 cm² (P < 0.0001) and median gradient decreased from 10 to 4 mmHg (P < 0.0001).

Figure 1 Cardiovascular survival without reintervention and without surgery alone, in the whole population. Kaplan–Meier rates are presented with standard errors.
This led us to compare the specific outcome between patients aged <50 and ≥50 years at the time of their initial PMC. Their baseline characteristics are compared in Table 1.

Cardiovascular survival without reintervention and cardiovascular survival without surgery alone are shown in Figures 3 and 4, respectively, for 504 patients aged <50 and ≥50 years at the time of their initial PMC. Events occurring during the follow-up are detailed in Supplementary material online, Table S3.

Repeat percutaneous mitral commissurotomy

Population

Of the 351 patients in whom a reintervention was indicated during the follow-up, 85 (24%) underwent a repeat PMC and 266 (76%) underwent surgery. Characteristics of the patients who underwent a repeat PMC are compared with those of surgically treated patients in Table 3. Patients who underwent a repeat PMC were younger, less frequently in atrial fibrillation and had less calcified valves than surgically treated patients. Finally, there were no
differences between the two groups regarding either NYHA functional class or the severity of mitral stenosis.

Results
There was no procedural mortality in repeat PMC. The most frequent complication was severe traumatic mitral regurgitation in three patients (4%). After repeat PMC, the median valve area increased from 1.1 to 1.9 cm² (P < 0.0001) and median gradient decreased from 10 to 4 mmHg (P < 0.0001). Good immediate results of repeat PMC, as previously defined, were obtained in 80 (94%) of the 85 patients.

During a median follow-up of 40 months (interquartile range 11–86) after repeat PMC, 2 patients died from cardiovascular cause and 27 patients underwent subsequent reintervention. Surgery, which consisted of mitral valve replacement in all cases, was performed in 23 patients, accounting for 85% of reinterventions: in 5 cases following poor immediate results of repeat PMC and in 18 cases because of iterative restenosis. A third PMC was performed in 4 patients, accounting for 15% of reinterventions. Of the 56 patients who were alive and did not need a further reintervention, 54 (96%) were in NYHA class I or II at the last follow-up.

After repeat PMC, the 10-year rate of cardiovascular survival without any further reintervention was 52 ± 8% and increased to 60 ± 7% when analysing cardiovascular survival without surgery alone.

Discussion
This series analysing reinterventions after PMC shows that 46% of patients remain free from cardiovascular death and surgery at 20 years. Repeat PMC was performed in one out of four patients presenting with mitral restenosis, of whom 60% remained free from surgery after 10 years, with few or no symptoms in most cases.

Population
Few series have reported follow-up beyond 15 years, and most of them included a majority of patients with favourable characteristics. The interest of the present series is to include patients with diverse characteristics, who represent a more heterogeneous group than young patients from developing countries or series with old patients. This is attested by the median age of 48 years and the fact that only 15% of patients had favourable valvular anatomy.

This series focused on patients with good immediate results of PMC. Poor late results after PMC may be related to the continuation of poor immediate results or to late deterioration after a successful procedure. Poor late results after poor immediate results are a consequence of insufficient valve opening or severe traumatic mitral regurgitation. Conversely the mechanism of late deterioration after good immediate results is generally related to

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Table 3  Comparison of the characteristics of the patients who underwent reintervention according to treatment by repeat PMC or surgery

<table>
<thead>
<tr>
<th>Variables</th>
<th>Repeat PMC (n = 85)</th>
<th>Mitral surgery (n = 266)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median [IQR] or n(%)</td>
<td>Median [IQR] or n(%)</td>
<td></td>
</tr>
<tr>
<td>Age, year</td>
<td>40 [32–46]</td>
<td>50 [42–57]</td>
<td>&lt;0.0001</td>
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<td>Female sex</td>
<td>74 (87)</td>
<td>214 (80)</td>
<td>0.17</td>
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<td>NYHA functional class</td>
<td></td>
<td></td>
<td>0.22</td>
</tr>
<tr>
<td>I–II</td>
<td>23 (27)</td>
<td>55 (21)</td>
<td></td>
</tr>
<tr>
<td>III–IV</td>
<td>62 (73)</td>
<td>211 (79)</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>23 (27)</td>
<td>108 (41)</td>
<td>0.025</td>
</tr>
<tr>
<td>Previous commissurotomy</td>
<td>23 (27)</td>
<td>44 (17)</td>
<td>0.03</td>
</tr>
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<td>Left atrial diameter (mm)</td>
<td>47 [44–50]</td>
<td>49 [45–54]</td>
<td>0.04</td>
</tr>
<tr>
<td>Valve area (echocardiography), cm²</td>
<td>1.1 [0.9–1.2]</td>
<td>1.0 [0.9–1.2]</td>
<td>0.55</td>
</tr>
<tr>
<td>Valve anatomy</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Class 1</td>
<td>20 (24)</td>
<td>29 (11)</td>
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<tr>
<td>Class 2</td>
<td>53 (62)</td>
<td>133 (50)</td>
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<tr>
<td>Class 3</td>
<td>12 (14)</td>
<td>104 (39)</td>
<td></td>
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<tr>
<td>Extent of valve calcification</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>0</td>
<td>73 (86)</td>
<td>162 (61)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10 (12)</td>
<td>64 (24)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1 (1)</td>
<td>27 (10)</td>
<td></td>
</tr>
<tr>
<td>3–4</td>
<td>1 (1)</td>
<td>13 (5)</td>
<td></td>
</tr>
<tr>
<td>Time between initial PMC and reintervention (months)</td>
<td>117 [75–161]</td>
<td>95 [55–145]</td>
<td>0.03</td>
</tr>
</tbody>
</table>

IQR, interquartile range.
progressive mitral restenosis. In a previous analysis of the same cohort, mitral restenosis was present in 97% of patients with late deterioration. We then chose to restrict the analysis to patients who had good immediate results of PMC in order to ensure homogeneity in the mechanism of late deterioration.

Events during long-term follow-up

In the present series, overall survival was 75% 20 years after good immediate results of PMC. This illustrates the low mortality rate of mitral stenosis after intervention.

After a successful PMC, mitral restenosis is the major cause of re-intervention and is becoming a frequent presentation of mitral stenosis in Western countries, due to the decreased incidence of rheumatic heart disease. When surgery is needed for restenosis, mitral valve replacement is frequently carried out due to frequent non-favourable valve anatomy and is the favoured therapeutic option for most teams. Patients are therefore exposed to perioperative morbidity and mortality and to long-term prosthetic-related complications. An alternative could be to repeat surgical commissurotomy, which has been shown to be feasible, but exposes patients to iterative thoracotomy. Randomized series comparing surgical commissurotomy and PMC did not specifically concern restenosis, but they did not find differences between the two techniques.

This raises the problem of choice of the most appropriate technique for restenosis treatment: either beginning with PMC and using surgery in case of procedural failure or in case of late deterioration or performing surgery as the first line treatment.

In the present series, the 20-year event-free survival rate was 38% for cardiovascular survival without any intervention and increased to 46% for cardiovascular survival without mitral surgery. The endpoint of mitral surgery has not been previously studied and its analysis shows that almost half of the patients presented initially with non-ideal anatomical conditions. In the subgroup of the 504 patients under the age of 50 at the time of their initial PMC, cardiovascular survival without re-intervention was 45% at 20 years and increased to 57% when analysing cardiovascular survival without surgery alone. This suggests that repeat PMC may be particularly useful for deferring the need for surgery in young patients.

Results of repeat percutaneous mitral commissurotomy

Repeat PMC was performed in one out of four patients with restenosis in our series and provided good immediate results in 94% of them, these rates being comparable to those obtained after a first PMC. The 10-year rate of 60% cardiovascular survival without surgery corresponds to the longest follow-up reported after repeat PMC.

These satisfactory findings may be related to the fact that we selected potential candidates for repeat PMC with a high likelihood of good immediate results given their anatomical and/or clinical characteristics. This is illustrated by the more favourable characteristics of patients who underwent repeat PMC (younger age, more frequent sinus rhythm, and more suitable valve anatomy) compared with those who received surgical treatment.

With regards to patient selection for repeat PMC, it is possible to propose the following steps. The usual contraindications to PMC must be respected. Repeat PMC can be used only in case of bicommissural refusion. Except for these points, the results of the present study support a wide use of repeat PMC given the low rate of complication and the good long-term results of the technique. Repeat PMC is particularly effective in delaying surgery in young patients and should be considered even in the case of non-ideal anatomical conditions. Finally, patients should be carefully followed to allow for timely surgery when needed.

Study limitations

A limitation of the present study is the absence of standardized echocardiographic follow-up due to the number and geographic localization of the patients. We could, therefore, neither analyse the anatomical mechanisms involved in secondary deterioration after successful PMC nor establish the exact rate of mitral restenosis.

The fact that 98 patients (11%) were lost to follow-up is the consequence of the mobility of young patients and of the length of follow-up. Patients lost to follow-up were younger and had higher mitral valve area after PMC, which may have led to a slight underestimation of event-free survival rates.

The present findings cannot be used to determine the most appropriate treatment in an individual patient presenting with mitral restenosis. Nevertheless, despite potential referral bias, this observational approach shows that the good long-term results of repeat PMC allow for further postponement of surgery in a substantial number of patients.

Conclusion

Although reintervention is frequently needed after successful PMC, long-term survival without surgery further illustrates the efficacy of this non-surgical procedure. According to selection criteria, repeat PMC was performed in one out of four patients who underwent mitral reintervention in our series, although the majority of patients presented initially with non-ideal anatomical conditions. The specific study of survival without mitral surgery shows the role of repeat PMC in delaying mitral surgery, with almost 50% of patients being free from surgery at 20 years. Freedom from surgery was even better in younger patients, in whom it is particularly attractive to postpone surgery when possible. These findings support the wide use of repeat PMC when feasible, particularly in young patients.

Supplementary material

Supplementary material is available at European Heart Journal online.
Conflict of interest: B.I. has received consultant fees from Servier, Boehringer Ingelheim, Bayer, Valtech, and Abbott, and speaker’s fees from Edwards Lifesciences, St Jude Medical and Sanofi-Aventis. D.H. has received consulting fees from Edwards Lifesciences and Medtronic. E.B. received consulting fees from Edwards Lifesciences. D.M.-Z. has received speaker’s fees from Edwards Lifesciences. A.V. is member of Advisory Board for Medtronic, Abbott, Valtech, and has received speaker’s fees from Edwards Lifesciences and Siemens. The other authors report no conflicts.

References


