Clinical research

Temporal trends in percutaneous mitral commissurotomy over a 15-year period

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Aims To evaluate temporal trends in percutaneous mitral commissurotomy (PMC) in terms of changes in patient characteristics and their impact on immediate results.

Methods and results From 1986 to 2001, PMC was indicated in 2773 consecutive patients. Patient characteristics and results were compared each year and linear trends were analysed. There were significant trends toward an increase in mean age (p < 0.0001) and the proportion of patients in NYHA class I or II before PMC (p < 0.0001), and toward a decrease in the proportion of atrial fibrillation (p < 0.002) and favourable valve anatomy (p < 0.0001), but no change in initial valve area (p < 0.22).

Technical failure occurred in 32 patients (1.2%). The failure rate decreased from 6.4% in 1986–1987 to 3.6% in 1988 and was less than 1.5% from then on (p < 0.0001). The frequency of good immediate results (valve area ≥ 1.5 cm² without regurgitation > 2/4) did not differ over the years (p < 0.22), with a mean rate of 89.5% of effective procedures and 88.5% of all procedures.

Conclusion Over this 15-year period, candidates for PMC became older and had a less favourable anatomy, but underwent PMC at an earlier functional stage. The stability of the results, despite the less favourable characteristics, may be related to the role of experience in improving the technique and patient selection.

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Introduction

Since percutaneous mitral commissurotomy (PMC) was first described by Inoue in 1984, the technique has been perfected and the short- and long-term results have led to an expansion of the indications.1–9 PMC is now considered to be the procedure of choice in patients with suitable valve anatomy.10 However, indications in patients with unfavourable anatomical conditions remain a matter of debate, which is particularly important in Western countries, where patients with rheumatic mitral stenosis are getting older and have more severely impaired valve anatomy.11,12

The impact of these temporal changes on patient demographics, technique, and indications of PMC have not yet been described.

We report the analysis of temporal trends in patient characteristics and results of PMC in a single-centre series over a 15-year period that corresponds to the onset and development of PMC.
Methods

Study population

Between March 1986 and December 2001, PMC was attempted in 2773 consecutive patients in our department. All patients had mitral stenosis with a valve area < 1.5 cm².

Contraindications were massive calcification or calcification of both commissures, left atrial thrombus on transoesophageal echocardiography, mitral regurgitation > grade 2/4, or the need for cardiac surgery because of severe aortic, tricuspid, or coronary disease.

Patient characteristics are described in Table 1. A total of 432 patients (15.6%) had undergone commissurotomy previously: closed commissurotomy in 263, open commissurotomy in 77, and PMC in 92; 27 patients (1.0%) had undergone aortic valve replacement previously.

Echocardiographic evaluation

Echocardiography was performed 24 h before PMC and 24–48 h after the procedure. Mitral valve anatomy was assessed by transthoracic echocardiography and fluoroscopy and classified into three groups, as previously described: pliable valves and mild subvalvular disease (group 1), pliable valves and extensive subvalvular disease (group 2), and calcified valves confirmed by fluoroscopy (group 3). The reference measurement for valve area was planimetry by two-dimensional echocardiography. If planimetry was not feasible, the Doppler pressure half-time was used instead. Mean mitral gradient was assessed by continuous-wave Doppler. Mitral regurgitation was quantified using colour Doppler. Mitral valve area was systematically used in 2125 patients, according to the stepwise technique under echo guidance.

Immediate results

When the procedure was effective, good immediate results from PMC were defined by a composite endpoint that associated a mitral valve area ≥ 1.5 cm² with no regurgitation ≥ 2/4.

Statistical analysis

All data were entered prospectively in a database beginning in 1986. Quantitative variables were expressed as means ± SD. To avoid important discrepancies in the number of procedures per year, the years 1986 and 1987 were considered together.

Pre- and post-procedural quantitative variables were compared with a paired t-test. The search for differences between years and temporal trends was performed in two steps. The first step was to search for differences in the distribution of variables between years using a one-way analysis of variance (ANOVA) for quantitative variables and a χ² test for qualitative variables. When ANOVA was significant for quantitative variables, a linear trend was sought using a linear model testing the significance of the slope estimate. When the χ² test was significant for qualitative variables, a linear trend was sought using a Cochran–Armitage trend test; when the test for trend was significant, the slope was estimated using linear regression. The estimation of the slope provided a quantitative interpretation of the magnitude of the trend, that is, the mean yearly increase (positive slope) or decrease (negative slope) of the dependent variable. All statistical tests were two-sided. A p-value < 0.05 was considered significant.

All analyses were made with SAS statistical software (SAS Institute Inc., release 8.2).

Results

Global results

Technical failure occurred in 32 patients (1.2%). This was related to hemopericardium in two cases, embolism in one, inability to cross the septum in eight, and inability to position the balloon across the valve in 20. Finally, a failure occurred in a pregnant patient, in whom the procedure was discontinued immediately after venous puncture because of foetal distress; she died during emergency caesarean section. In-hospital death occurred in 11 patients (0.4%). Aside from the pregnant patient mentioned above, death was caused by tamponade in two patients, stroke in one patient, and low-output in the remaining seven patients who were in critical haemodynamic condition before PMC, four of whom were aged ≥ 80 years. Other severe adverse events were tamponade in six patients (0.2%), arterial embolism with sequelae in 11 patients (0.4%), and severe mitral regurgitation grade ≥ 3/4 in 113 patients (4.1%). Surgery was performed in the first month following PMC in 130 patients (4.7%).
The differences between years and temporal trends in the total population of 2773 patients. Patient characteristics are shown in Table 2. This remained significant when restricting the analysis to French residents (p < 0.0001). Good immediate results were obtained in 2454 patients, 89.5% of the 2741 effective procedures and 88.5% of the total population of 2773 patients.

Temporal trends in patient characteristics

The differences between years and temporal trends in patient characteristics are shown in Table 2. The majority of patients originated from metropolitan France and included both French natives and immigrants (Fig. 1). The proportion of patients coming from foreign countries decreased progressively between 1986 and 2001 (Table 2).

Mean age differed over the years, with a significant linear trend toward an increase from 43 to 51 years. The mean annual increase for the proportion of patients in NYHA class I and II increased from 17.1% to 43.5%, only 1.7% being in class I (Fig. 2c, Table 2). The proportion of patients in atrial fibrillation before the procedure decreased according to a linear trend from 33.6% to 25.1% (Fig. 2b, Table 2).

The proportion of patients who had undergone previous commissurotomy varied between years but showed no consistent trend (Table 2).

There was a highly significant decrease in the proportion of patients with ideal anatomy (group 1), the mean annual decrease being 1.6%. Conversely, the proportion of patients with calcified valves was only 0.5% (group 3) (Fig. 2d, Table 2). There was a trend toward and increase in the proportion of preprocedural grade 1 or 2 mitral regurgitation (Table 2).

Temporal trends in immediate results of PMC

The rate of technical failure differed over time (p < 0.0001) and decreased with a significant linear trend (p < 0.0001, slope −0.00215 ± 0.00048). It was 6.4% in 1986–1987, 3.6% in 1988, and stabilised at < 1.5% after the systematic use of the Inoue stepwise technique was introduced (Fig. 3a).

In-hospital mortality differed between years (p < 0.02) but without a linear trend (p < 0.57). The rate of tamponade was 1.4% in 1986–1987 and then decreased to very low rates (p < 0.23) (Fig. 3a). The rate of thromboembolic events did not change over time (p < 0.39). Severe traumatic mitral regurgitation was the most frequent complication and its frequency remained stable over time (p < 0.36) (Fig. 3b). The proportion of patients operated on within the first month following PMC differed (p < 0.014) and decreased over time (p < 0.0025, slope −0.00287 ± 0.00095).

After PMC, mean valve area increased from 1.03 ± 0.23 cm² to 1.87 ± 0.30 cm² (p < 0.0001) and mean gradient decreased from 10.3 ± 4.6 to 4.8 ± 2.1 mm Hg (p < 0.0001). The proportion of patients who underwent PMC while in NYHA class III and IV decreased while the proportion of patients in NYHA class I and II increased from 17.1% to 43.5%, only 1.7% being in class I (Fig. 2c, Table 2).

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Pre- and post-procedural valve area and mean gradient are shown in Fig. 4a and b. There was no difference in pre-procedural valve area (p < 0.21), while post-procedural valve area differed \( p < 0.0001 \) and decreased significantly over the years \( p < 0.0001 \) for linear trend. However, the slope of the trend was \( -0.008 \pm 0.001 \text{ cm}^2 \), corresponding to a mean yearly decrease in the final mitral valve area of only 0.008 cm², and there was a trend toward an increase in final valve area after 1999. Pre-PMC mean mitral gradient significantly decreased. Mean gradient after PMC differed between years \( p < 0.001 \), but without any significant trend \( p < 0.70 \). Finally, the proportion of good immediate results, as assessed by the binary endpoint, did not differ over the years \( p < 0.22 \) (Fig. 5).
Discussion

This 15-year experience shows that important changes occurred in the characteristics of patients who were PMC candidates as a consequence of changes in epidemiology and practices. Despite significant trends toward increased age and less favourable anatomical conditions, the safety of the technique improved and its efficacy was maintained.

Global results

This study reports the results of PMC in a population originating mainly from a European country, with diverse clinical and anatomic characteristics of presentation. The safety of PMC has been confirmed by the low rates of technical failure and major adverse events. These results are consistent with large series from centres with experience, while certain multicentre series reported higher rates of failure and tamponade as a consequence of the inclusion of low-volume centres where physicians were initiating their experience. The efficacy is confirmed by the significant improvement in valve function, of a level similar to the results of other series from Western countries. Better results are observed in countries where rheumatic fever is still endemic and in which most patients are young and have favourable characteristics.

Temporal trends in patient characteristics

The high number of French residents in the present series is not related to the incidence of rheumatic fever, which has dramatically decreased in Western countries. It is more likely to be the consequence of the concentration of PMC procedures in a limited number of high-volume centres in European countries.

During this 15-year period, candidates for PMC became older. This may be explained by epidemiological changes, such as the decline in the incidence of rheumatic fever and the slower evolution of the disease in Western countries, as well as changes in practice involving a policy of expanding the indications for PMC. Increasing age and the expansion of indications for PMC explain the increase in the proportion of patients with unfavourable anatomy.

On the other hand, there was a trend toward performing PMC at an earlier stage of the disease. The objective was to reduce the hazards of subsequent haemodynamic and thromboembolic complications using a low-risk procedure. The increase in the proportion of patients in NYHA class I or II before PMC was highly significant in the present series, mainly because of patients in class II, while PMC was seldom performed in truly asymptomatic patients. These changes are consistent with the decrease in the proportion of patients in atrial fibrillation. However, less advanced functional status was not the result of performing PMC in patients with less severe mitral stenosis, as illustrated by the absence of change in pre-procedural valve area.

Temporal trends in immediate results of PMC

The sharp decrease in the number of technical failures may be interpreted in the light of the learning curve and improvements in the technique. This is also true for the
rapid decrease in the incidence of tamponade, with only three cases occurring during the last decade. For our team, the effect of the learning curve was significant for the first 50 cases.\textsuperscript{13,21} Since 1990 and the systematic use of the Inoue balloon, technical failure and tamponade are very rare. This may be related to experience and the technique used, since the Inoue technique is generally associated with lower rates of failure and tamponade than the double-balloon technique.\textsuperscript{14} There was no decrease in mortality but periprocedural deaths seem to be more related to patient characteristics than to complications inherent to the procedure itself.

Good immediate results, as assessed by a composite endpoint, were obtained in 89.5% of effective procedures (88.9% of all procedures) and there was no significant difference between years. When analysing each component of the composite endpoint, there was a small decrease in post-procedural valve area. Nevertheless, the trend toward a decrease in post-PMC valve area was only 0.008 cm\(^2\) per year, which is unlikely to be clinically relevant. On the other hand, there was no change in the frequency of severe traumatic mitral regurgitation, which occurred in 4.1% of the patients in our series and remains the most frequent complication of PMC, whatever the technique used.\textsuperscript{22,23} This illustrates the fact that, even when using a refined analysis of valve anatomy, the occurrence of severe mitral regurgitation remains difficult to predict in any given patient.\textsuperscript{22,24,25}

The stability of the immediate results despite the increase in age and higher frequency of anatomic valve impairment can be interpreted in the light of the multifactorial nature of the prediction of immediate results. The negative impact of increasing age and less favourable anatomy on the immediate results should be analysed according to the magnitude and predictive value of these changes.\textsuperscript{13,26,27} Mean age increase was moderate (0.7 year/year) and the trend toward less favourable valve anatomy was mainly related to the increase in the proportion of patients in echocardiographic group 2 and the decrease in patients in group 1. The increase in the proportion of patients in group 3 (calcified valves), which has the most negative impact on immediate results, was less pronounced and of borderline significance. On the other hand, the proportion of previous commissurotomy, which has a particularly negative impact on the immediate results when combined with increasing age, did not change over time. Initial valve area is another strong predictor of poor immediate results, and mean initial valve area did not vary in the present series. Conversely, the use of the Inoue balloon has a positive impact on the composite endpoint of good immediate results and this may partly compensate for less favourable patient characteristics.\textsuperscript{13} Moreover, it has been suggested that the impact of impaired valve anatomy was reduced with the use of the Inoue balloon.\textsuperscript{28}

Following the interpretation of previously identified predictors, our policy was to expand indications of PMC to patients who did not meet adequate anatomic conditions when their other characteristics were favourable. However, this did not result in the systematic performance of PMC in patients with unsuitable anatomic conditions, as attested by the limited increase in the proportion of valve calcification and the stability of the proportion of previous commissurotomy and pre-PMC valve area.\textsuperscript{13,26,27} Patient selection oriented by previously identified predictors of immediate results may account for the continuing high rate of good immediate results despite increasing age and less favourable valve anatomy.

Limitations of the study

Comparison with other studies may be limited by the different methods used to evaluate mitral anatomy. The classification that we used from the beginning is based on the selection of patients for the most appropriate surgical procedure and it is recognised as a suitable method for assessing valve anatomy in mitral stenosis.\textsuperscript{10}

It was not possible to assess the respective impact of changes related to PMC epidemiology or indications. Our approach was pragmatic and the purpose was to describe and evaluate the global impact of changes that occurred simultaneously and contributed to changes in the presentation of patients with mitral stenosis in a Western country.

The extrapolation of our results may be limited and a referral bias cannot be excluded. This is inherent to any series from a specialised centre. On the other hand, a high and relatively stable number of annual procedures, together with the homogeneity of the evaluation performed in a single centre, are required to analyse accurately differences over the years and to search for temporal trends with an adequate statistical power.

The analysis of temporal trends over a long period and their impact on the late results observed would have required a particularly long observation time, which was beyond the scope of the present study. From the previous identification of predictors of late outcome, it could be expected that the negative effect of changes in age and valve anatomy would be compensated by earlier performance of PMC and the stability of immediate results.\textsuperscript{9}

Finally, the number of univariate tests performed in the present study leads to an increase of type I errors that are inherent to the exploratory approach testing for multiple variables. However, it should be stressed that the majority of differences and trends were highly significant and it is unlikely that such associations would have resulted from chance alone.

Conclusion

This series confirms the safety and efficacy of PMC when performed at centres with experience. The analysis of temporal trends over a 15-year period shows that candidates for balloon commissurotomy were getting older and had more severely impaired valve anatomy, but they underwent the procedure at an earlier functional stage. The increased safety and stability of the results may be interpreted as a consequence of the improvement in the
Temporal trends in percutaneous technique and patient selection based on previously identified predictors. These findings illustrate the adaptation to the changing pattern of mitral stenosis in Western countries and confirm the usefulness of PMC in the treatment of a wide range of patients with mitral stenosis.

References