Rheumatic fever recurrence: a possible cause of restenosis after percutaneous mitral valvuloplasty

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Background. **We evaluated the occurrence of a rapid process of restenosis after percutaneous mitral valvuloplasty (PMV), initiated by the recurrence of acute rheumatic fever. Restenosis after PMV has been mainly related to a high echocardiographic score (≥ 8) indicating a severely compromised mitral valve apparatus.**

Methods. **From 1986 to 1996, 120 patients underwent PMV by the transseptal approach at our Institution. The mean follow-up time was 58 ± 32 months (range 3 months to 9 years).**

Results. **Restenosis occurred in 10 patients (8.3%): in 4 restenosis was found within a relatively short period of time (1 to 3 months) following a documented recurrence of acute rheumatic fever; in the other 6 patients there was a gradual loss of the initial gain in the mitral valve area.**

Conclusions. **These data suggest two potential mechanisms of restenosis: l) a more common slow process, due to turbulent flow-trauma on the mitral valve; 2) a rapid process that relates to valvulitis consequent to a recurrence of acute rheumatic fever. In consideration of the second possibility, after PMV prophylactic treatment may be warranted at least in those patients who are at high risk of streptococcal infection.**

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Introduction

Percutaneous mitral valvuloplasty (PMV) is a widely accepted treatment for mitral stenosis and constitutes a valid alternative to surgical commissurotomy[1].

Restenosis after PMV, commonly defined as a loss of 50% or more of the initial gain in the mitral valve area, has been reported to occur in 4 to 27% of patients with calcification[2], and in up to 46% of patients with significantly calcified mitral valves[3]. An echocardiographic score[4] > 8, which indicates a severely compromised mitral valve apparatus, has been shown to be an independent predictor of restenosis[5]. This is also thought to be a consequence of the less favorable immediate outcome of PMV associated with this condition.

The present study shows that recurrence of acute rheumatic fever after PMV may initiate a process of restenosis, which appears to be quite rapid as distinct from the more common gradual loss of the acute gain in valve area that finally reaches clinical significance.

Methods

The study population consisted of 120 patients who underwent PMV by the transseptal approach at our Institution from October 1986 to November 1996. There were 78 women and 42 men. The patients' age ranged from 14 to 73 years with a mean of 45 ± 14 years. Eighty-one patients were in normal sinus rhythm and 39 in atrial fibrillation. A thorough clinical evaluation, including an echocardiographic study, was performed in all patients before PMV.

Technique. In the first 27 patients, PMV was performed using the double-balloon technique[6], and in the remaining cases using the Inoue single-balloon technique. Right heart catheterization was achieved via the right femoral vein and retrograde left heart catheterization via the left femoral artery. Heparin (5000 IU) was given immediately after transseptal catheterization. Basal hemodynamic data were obtained. Then, left ventriculography was performed to evaluate mitral competence

and the subvalvular apparatus. After mitral balloon dilation, hemodynamic evaluation was repeated, followed by a complete oximetry series for the detection of a possible left-to-right shunt, and by control left ventriculography.

The mitral valve area was calculated using the Gorlin formula[7].

Follow-up. A complete clinical evaluation including echo-Doppler study was performed in all patients 24 hours after the procedure, and again at 1, 3 and 6 months of follow-up; then, all patients were submitted to clinical evaluation every 6 months up to 3 years, and every year thereafter. No patient was lost to follow-up.

The mean follow-up was 58 ± 32 months (range 3 months to 9 years). Restenosis was defined as a loss of at least 50% of the initial gain in the mitral valve area.

Statistical analysis. Data were analyzed using the Student's t test for unpaired data.

Results

After PMV, there was a decrease in the mean transmitral gradient from 18.1 ± 7.2 to 9.1 ± 6.8 mmHg ($p < 0.001$) and in the mean pulmonary artery pressure from 30.9 ± 8.4 to 22.9 ± 8.7 mmHg ($p < 0.05$). There was also a significant increase in the cardiac output from 4.5 ± 1.2 to 5.13 ± 1.4 l/min ($p < 0.05$) and in the valve area from 1.1 ± 0.3 to 1.9 ± 0.5 cm^2 ($p = 0.001$). Complications of the procedure included 2 cases (1.6%) of severe mitral regurgitation submitted to elective mitral valve replacement within 1 month and 1 case (0.8%) of a cerebrovascular accident 6 hours after PMV. In no case did we observe a significant left-to-right shunt (QP/QS ≥ 1.5) following PMV[8].

Follow-up. Two patients (1.7%) died: one within 2 weeks of PMV due to broncho-pneumonic complications and the other, who had also undergone coronary angioplasty of the circumflex artery a few days after PMV, died suddenly 1 year later.

Six patients (5%) underwent mitral valve replacement either for mitral regurgitation or restenosis.

Restenosis, as identified at echocardiography and/or cardiac catheterization, occurred in 10 patients (8.3%). In 4 of these (3.3%) restenosis occurred within a relatively short period of time (1 to 3 months) following a documented recurrence of acute rheumatic fever. All 4 patients (2 males and 2 females) were hospitalized for acute rheumatic fever during the acute episode; the diagnosis was made on the basis of the modified Jones criteria. The time intervals from PMV to the recurrence of rheumatic fever were 7, 18, 17 and 24 months, respectively. The last echo-Doppler study, performed 2 to 3 months before the acute episode, had revealed that there were no significant changes in the mitral valve area with respect to the immediate results of PMV. Table I shows the changes in mitral valve area in each patient both before and after PMV as well as before and after the recurrence of rheumatic fever. All 4 patients were successfully resubmitted to PMV within 1 to 4 months of the diagnosis of restenosis.

In the other 6 patients, a gradual loss of the initial gain in the mitral valve area was observed. The time interval which elapsed before the point of restenosis was 3 to 7 years (mean 56 ± 17 months). These patients underwent either re-PMV (2 cases) or mitral valve replacement (4 cases).

Discussion

The different time course in the development of restenosis occurring in 10 of 118 surviving patients submitted to PMV seems to suggest two pathophysiological mechanisms of restenosis. A more common slow process taking years is a consequence of the progression of valvular fibrosis leading to calcification and is probably due to the turbulent flow-trauma. If the mitral valve apparatus is severely compromised and the gain in the mitral valve area after PMV less than adequate, a significant turbulent flow-trauma would result. Thus, the probability of restenosis is increased. On the other hand, it has been shown that a pre-procedural

Table I. Rapid loss in mitral valve area after rheumatic fever recurrence in 4 patients.

Patient	Sex	Age (years)	Time PMV-RFR (months)	MVA (cm^2)			
				Pre-PMV	Post-PMV	Pre-RFR	Post-RFR
1	M	21	7	1.1	3.2	3.1	1.5
2	M	42	18	0.7	1.7	1.6	0.9
3	F	38	17	1.04	2.3	2.1	1.0
4	F	41	24	1.1	1.9	1.7	0.7

MVA = mitral valve area; PMV = percutaneous mitral valvuloplasty; RFR = rheumatic fever recurrence.

echocardiographic score ≤ 8, which means a moderately compromised mitral valve apparatus, and a post-procedural mitral valve area ≥ 2 cm^2 are both predictors of a good long-term outcome after PMV[2]. Moreover, the immediate outcome of PMV is largely dependent on the pre-procedural status of the mitral valve[9]: a severely altered mitral valve apparatus (high echocardiographic score) may yield a modest gain in valve area and such conditions favor the onset of the slow process of restenosis.

Rheumatic fever recurrence may initiate a rapid process of restenosis, as demonstrated in 4 of our patients. It is well known that after an episode of rheumatic fever, the development of mitral valve obstruction takes a long period of time; however the process may be accelerated by a new episode of acute rheumatic valvulitis which enhances commissural fusion and thickening of the mitral leaflets and subvalvular apparatus. The rapid loss in mitral valve area, occurring in our patients after the episode of acute rheumatic fever, may be largely attributed to re-fusion of the commissures. Obviously there is no direct evidence implicating acute valvulitis as the etiological factor of restenosis; however this pathophysiological mechanism should be considered highly probable.

In view of this possible cause of restenosis after PMV, prophylactic treatment may be warranted in patients who are at high risk of streptococcal infection.

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