A comparison of rate control and rhythm control in patients with atrial fibrillation after percutaneous mitral balloon valvotomy: a randomized controlled study

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Abstract

Objective: To compare rate-control and rhythm-control strategy in patients with atrial fibrillation (AF) after percutaneous mitral balloon valvotomy (PMV).

Patients and interventions: We conducted the prospective, randomized trial in 183 patients with AF after successful PMV and AF duration (AFD) ≤ 12 months, post-PMV left atrial size (LA) ≤ 45 mm. The primary endpoint was improvement in atrial-fibrillation-related symptoms. Other secondary study endpoints included 6 min walking tests, Quality of life (QOL), normalization of LA, the number of hospital admissions and the duration of hospital stay.

Results: Over one year, 2% patients in the rate-control group had sinus rhythm, as compared with 96% of patients in the rhythm-control group (p < 0.001). A greater proportion of patients reported improvement in symptoms in rhythm-control group than in rate-control group (at every visit time, p < 0.0001, respectively). Walking distance in a 6 min walk test, QOL and LA normalization was better in rhythm-control group compared with rate-control group. The strategy of rhythm control was associated with similar times of hospital admissions, but longer duration of hospital admissions. There was no difference in drug-related side effect as compared rate-control group with rhythm-control group. During the follow-up period, neither embolic nor transitory ischemic neurological events occurred in both groups.

Conclusions: In patients with AF after PMV, AFD ≤ 12 months and post-PMV LA ≤ 45 mm, sinus rhythm could be easy and safe to achieve and maintain, moreover, patients benefited from restoration and maintenance of sinus rhythm in terms of improvement in atrial-fibrillation-related symptoms, 6 min walking tests, QOL and LA normalization. Rhythm control should therefore be considered as the preferred initial therapy in this group of patients. The optimal strategy to treat AF after PMV should be individualized.

Key Words: atrial fibrillation • antiarrhythmia agents • electrocardioversion • mitral stenosis • valvuloplasty

Abbreviations: AF, atrial fibrillation; PMV, percutaneous mitral balloon valvotomy;
AFD, AF duration; LA, left atrial size; QOL, Quality of life

Most of patients with rheumatic mitral valvular stenosis and atrial fibrillation (AF) remain in AF rhythm after percutaneous mitral balloon valvotomy (PMV). AF can adversely affect hemodynamics. The absence of atrial systole (atrial kick) and a rapid ventricular rate with relative shortening of diastole can increase left atrial pressure, worsen pulmonary venous congestion and compromise cardiac output. Moreover, stasis of blood in the left atrial appendage predisposes to development of thrombi and embolic complications. AF also generates significant health care costs.

Sinus rhythm is difficult to achieve and maintain in patients with rheumatic mitral valvular stenosis and AF, but would be more easily achieved with reduction of left atrial pressure after successful PMV. In our previous study, we found longer atrial fibrillation history, smaller mitral valve area and higher left atrial pressure after PMV are the key factors of atrial fibrillation recurrence. Sinus rhythm can maintain in a higher proportion of patients with AF duration (AFD) ≤ 12 months, post-PMV LA ≤ 45 mm than those with AFD > 12 months, post-PMV left atrial size (LA) > 45 mm. This indicates that rhythm control may be prior to rate control in this selected group patients.

At present, there are not prospective data that compare strategies of rate control and rhythm control in patients with AF after PMV. The optimal strategy to treat the condition has not been established yet. This prospective randomized trial was designed to examine this important clinical issue.

METHODS

Study population
This study was designed as a prospective, randomized, single-center clinical trial to compare strategies of rate control and rhythm control in patients with AF after successful PMV with the Inoue technique. A successful procedure is defined as PMV achieved without acute mitral valve replacement, and a mitral valve area after PMV of ≥1.5 cm². Transesophageal echocardiography was done one day before PMV. AF was identified by electrocardiography (ECG). If another ECG done during 12 months before PMV showed the presence of sinus rhythm, the AFD was defined as ≤ 12 months. Patients who remained in AF rhythm 3 days after PMV, with AFD ≤ 12 months and post-PMV LA ≤ 45 mm were eligible if they could give written informed consent. Patients were excluded from the study if they had received antiarrhythmic therapy within 5 half-lives of the time of random assignment. Recruitment began from March 1, 2001 and randomization was concluded in March 30, 2004. Three days after PMV, patients recruited for this pilot study were randomly assigned to one of two following treatment arms.

In rate-control group, no attempt was made to terminate atrial fibrillation. Rate control was achieved with the administration of digitalis, a nondihydropyridine calcium-channel blocker, and a beta-block, alone or in combination. Rate control during AF was assessed both at rest and during activity. The target was a resting heart rate of 60 to 80 beats per minute and 90 to 115 beats per minute during moderate exercise. If patients had intolerable symptoms due to atrial fibrillation, unacceptable adverse effects of the atrioventricular-node-blocking or the control of ventricular response could not be achieved despite treatment, cardioversion was performed;
In rhythm control group, antiarrhythmic drug therapy with or without electrical cardioversion aimed at restoration of sinus rhythm. Preferred initial treatment used amiodarone at a daily dose of 600 mg for 1 week. If sinus rhythm had not been restored within 1 week, patients were electrically cardioverted followed by administration of low-dose amiodarone (100-200 mg daily) aimed at prevention of recurrent atrial fibrillation at the lowest effective level. In case of recurrent atrial fibrillation, restoration of sinus rhythm was repeated in two weeks as above.

Both randomization groups received adequate anticoagulation with a target international normalized ratio [INR] of 2.0–3.0. If sinus rhythm was present at one month, the oral anticoagulant could change to aspirin (300 mg daily).

This trial was done at Renmin Hospital of Wuhan University, P.R.China. Research and Ethics Committee of Wuhan University proved this protocol. Written informed consent was obtained from all patients.

Clinical follow-up
All randomized patients were followed for 12 months with regular visits scheduled for 3 days (baseline), 3 weeks, and 3, 6, and 12 months after PMV. Upon hospital discharge, patients were given diaries to list symptoms, follow-up physician appointments, and rehospitalization. Patients were advised to call at any time if they experienced new symptoms.

Study procedure
At baseline and at follow-up visits, patients underwent one-dimensional and two-dimensional echocardiography, a 6 min walk test, and assessment of the QOL. Laboratory studies to assess liver and thyroid function and chest radiographs should be performed at least every six months.

Endpoints
Since patients underwent PMV usually are mostly young patients in Mainland China\(^9\) and AF is usually not life-threatening, the endpoints excluded death in this short-term study. The primary endpoint was improvement in atrial-fibrillation-related symptoms in symptomatic AF. Other secondary study endpoints included 6 min walking tests, Quality of life (QOL), normalization of LA, the number of hospital admissions and the duration of hospital stay (measured from date of admission to discharge). Improvement in atrial-fibrillation-related symptoms in symptomatic AF was assessed during each follow-up visit by the changes compared with baseline in the three most frequently reported symptoms-palpitations, dyspnoea, and dizziness.\(^{10}\) Symptomatic improvement was defined (in hierarchical order) as either an elimination of palpitations (if present at baseline), or a reduction in the frequency of episodes of dyspnoea (if palpitations were not eliminated), or a reduction in the frequency of dizzy spells (if palpitations were not eliminated and dyspnoea was unchanged). In cases where no palpitation was present at baseline, symptomatic improvement was defined as continued absence of palpitations and an improvement in dyspnoea or dizziness, as described above. These symptoms were carefully assessed by interviews in every patient. Another common atrial-fibrillation-related symptom is “easy fatigability”. However, this symptom was separately assessed by 6 min walking tests.\(^{10}\)
Assessment of the Health-Related QOL (HRQOL)

Patients completed the MOS Short Form-36 (SF-36) at baseline and after 12 months. It measured the multidimensional properties of the HRQOL on a scale ranging from 0 to 100, with lower scores representing a lower QOL. The SF-36 is a standardized, generic HRQOL measurement instrument that has been validated in the Chinese population.

Statistical analysis

Statistical analysis was performed using the intention-to-treat principle. Continuous variables were expressed as mean ± SD. Categorical variables were presented by frequencies and percentages. Significance was assumed with a two-sided p-value of below 0.05. We tested continuous variables by One-Way ANOVA for between-group comparisons (with the baseline value as the covariable) and Student’s t-test for within-group comparisons. If a normal distribution of variables was not presents, the Mann-Whitney Test was used for testing treatment-group differences and the Wilcoxon signed ranks test for testing within-group differences. Group comparison for categorical variables was performed by the chi-squared test with continuity correction or Fisher’s exact test as appropriate. The data were analyzed using SPSS for windows 11.0 (SPSS inc.).

The sample size was calculated using Power And Precision (release 2.00, Biostat Inc.). It was calculated on the assumption that symptoms could be improved by rate control in 50% of individuals with symptomatic AF; by contrast, rhythm control was estimated to be effective in 80% of individuals. In order to detect significant differences between the two treatment strategies, fifty-two patients with symptomatic AF after PMV should be included in each treatment group to achieve a power of 90% at 95% confidence levels (two-sided).

RESULTS

Characteristics of patients

A total of 183 consecutive eligible patients who consented to participate in the study were recruited. There were 122 females and 61 males, aged 36.9 ± 5.4 years (range 25-56 years). They had chronic AF for an average of 158.7 ± 120.3 days (range 28-365 days) and the mean post-PMV LA size (anteroposterior dimensions) was 39.9 ± 3.9 mm (range 32–45 mm). 91 patients were randomly assigned to rate-control strategy and 92 to rhythm-control strategy. 52 patients with symptomatic AF were included in rate-control strategy and 58 in rhythm-control strategy. The baseline characteristics in the two groups with respect to age, sex, AFD, AF-related symptoms, post-PMV echocardiography parameters, and pharmacological therapy were similar (Table 1).

Table 1. Baseline characteristics of eligible patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rate control (n=91)</th>
<th>Rhythm control (n=92)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>37.3±6.4</td>
<td>36.5±4.2</td>
<td>0.34</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>59(64.8)</td>
<td>63(68.5)</td>
<td>0.60</td>
</tr>
</tbody>
</table>
Mean AF duration, days 160.9±122.2 156.5±119.0 0.81
AF-related symptoms, n (%) 52(57.1) 58(63.0) 0.42
   Palpitation, n (%) 38(73.1) 37(63.8) 0.30
   Dyspnoea, n (%) 32(61.5) 30(51.7) 0.30
   Dizziness, n (%) 5(9.6) 6(10.3) 0.90
AF-related symptoms, n (%)

Post-PMV Echocardiography parameters
LA size, mm 39.8±4.1 40.0±3.7 0.80
MVA, cm² 1.84±0.15 1.81±0.16 0.21
MLAP, mmHg 11.9±2.8 12.5±2.7 0.13

Pharmacological therapy, n%
   Digoxin 80(87.9) 82(89.1) 0.80
   β-blockers 15(16.5) 20(21.7) 0.37
   Diltiazem 9(9.9) 15(16.3) 0.20
   Aspirin 88(96.7) 85(92.4) 0.20
   Anticoagulation agents 12(13.2) 9(9.8) 0.47
   Nitrates 36(39.6) 28(30.4) 0.20
   Diuretics 45(49.5) 54(58.7) 0.21

Values are mean±SD or n (%); AF indicates atrial fibrillation; PMV, percutaneous mitral balloon valvotomy; MVA, mitral valve area; LA, left atrium; MLAP, mean left atrium pressure.

Therapy
None of the patients was lost to follow-up and no death occurred during the course of study. In rate-control group, digoxin was used initially in nearly 58% of patients. 73% of patients required 2 drugs to achieve adequate rate control. Cardioversion was performed in 5 (5.5%) patients: 1 patient had intolerable symptoms due to AF, 3 patients with unacceptable adverse effects of the atrioventricular-node-blocking and 1 patient in whom the control of ventricular response could not be achieved despite treatment.

In rhythm-control group, pre-treatment with amiodarone resulted in pharmacological restoration of sinus rhythm in 26% of patients prior to electrical cardioversion. In the remaining patients, at least one electrical cardioversion had been done: 6% of patients twice and 2% three times. The cardioversion success rate was 100%. The mean amiodarone maintenance dose was 130 mg/day (87) at 24 weeks and 121 mg/day (56) at 52 weeks. In rate-control group, only 2% patients were in sinus rhythm at the end of the observation period compared with 96% patients in rhythm-control group (p < 0.001, Figure 1)

Only 5 (5.5%) patients crossed over from rate control to rhythm control and 3 (3.3%) patients from rhythm control to rate control (p = 0.72).

Primary endpoint
A greater proportion of patients reported improvement in symptoms in rhythm-control group than in rate-control group at every visit time. There were significant differences in terms of the primary endpoint between both groups at any point during the course of the
Exercise tolerance
There were significant differences between the two treatment strategies as measured by the 6 min walk test (baseline: p=0.57; first visit: p<0.0001; second visit: p<0.0001; third visit: p=0.02; fourth visit: p=0.01, Figure 3).

Quality of life
The scores of the eight subscales of the SF-36 were similar in the two groups at baseline. However, QOL scores were significantly lower than those reported from healthy individuals. At one year, most measures have improved and the rhythm-control group showed a greater improvement in QOL scores compared to the rate-control group (Table 2).

Table 2. Assessment of quality of life (SF-36)

<table>
<thead>
<tr>
<th>SF-36 Variable</th>
<th>Rate control</th>
<th>Rhythm control</th>
<th>P</th>
<th>China Nom*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical functioning</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>54.8±17.2</td>
<td>52.3±19.0</td>
<td>0.06</td>
<td>82.2</td>
</tr>
<tr>
<td>Month 12</td>
<td>67.8±36.9†</td>
<td>80.9±27.1‡</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td><strong>Physical role function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>42.0±19.2</td>
<td>39.2±20.8</td>
<td>0.4</td>
<td>81.2</td>
</tr>
<tr>
<td>Month 12</td>
<td>57.1±15.6‡</td>
<td>74.3±21.0‡</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td><strong>Bodily pain</strong></td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>58.5±22.4</td>
<td>61.0±25.1</td>
<td>0.8</td>
<td>81.5</td>
</tr>
<tr>
<td>Month 12</td>
<td>70.4±26.4‡</td>
<td>79.4±20.3‡</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td><strong>General health</strong></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>36.3±38.3</td>
<td>34.6±35.1</td>
<td>0.9</td>
<td>56.7</td>
</tr>
<tr>
<td>Month 12</td>
<td>38.5±43.1</td>
<td>52±42.8†</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td><strong>Vitality</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>35.3±12.8</td>
<td>33.4±15.5</td>
<td>0.7</td>
<td>52.0</td>
</tr>
<tr>
<td>Month 12</td>
<td>41.0±19.2†</td>
<td>49.5±20.1†</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td><strong>Social functioning</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>61.2±43.1</td>
<td>63.6±36.0</td>
<td>0.5</td>
<td>83.0</td>
</tr>
<tr>
<td>Month 12</td>
<td>73.2±32.4†</td>
<td>79.1±28.4‡</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td><strong>Emotional role function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>64.4±35.3</td>
<td>65.4±34.2</td>
<td>0.9</td>
<td>84.4</td>
</tr>
<tr>
<td>Month 12</td>
<td>66.3±27.3</td>
<td>75.6±28.1†</td>
<td>0.06</td>
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<tr>
<td><strong>Mental health</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>39.0±19.1</td>
<td>37.7±21.0</td>
<td>0.7</td>
<td>59.7</td>
</tr>
<tr>
<td>Month 12</td>
<td>47.6±18.3†</td>
<td>54.1±18.0‡</td>
<td>0.04</td>
<td></td>
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</table>
SF-36 scores presented as mean± SD scores; * Data from general population of Hangzhou, Mainland China assessed by SF-3616; † p < 0.05 for within-group difference from baseline; ‡ p < 0.01 for within-group difference from baseline.

The normalization of LA size
In comparison with baseline, significant (p < 0.0001, respectively) reductions of LA dimension were noted at one year in rate-control group (39.8 ± 4.1 to 36.4 ± 3.6 mm) and rhythm-control group (40.0 ± 3.7 to 33.5 ± 3.8 mm). The rhythm-control group showed a greater decrease in LA size compared to the rate-control group (6.4 ± 3.8 vs. 3.4 ± 2.8 mm, respectively; p < 0.0001). The normalization of LA size (LA size ≤ 30 mm) at follow up was seen in 14.4% of 90 patients in rhythm-control group, but in 1.1% of 88 patients in rate-control group (p < 0.001).

Thromboembolic prophylaxis and embolic or ischemic neurological events
In rate control arm, oral warfarin was used as thromboembolic prophylaxis in 54.9% patients. Aspirin and ticlopidine were used in 34.1% and 5.5% of patients, respectively. In rhythm-control group, 76.9% patients received warfarin therapy for one month before sinus rhythm was present. In 81.5% of study subjects, thromboembolic prophylaxis was continued with aspirin, and 3.3% of patient received ticlopidine. During the follow-up period, neither embolic nor transitory ischemic neurological events occurred in both groups.

Adverse effects
There was no difference in adverse event rate between groups. At least one drug-related side-effect was seen in 15 (16.5%) out of 91 rate-control patients compared with 10 (10.9%) out of 92 rhythm-control patients (p=0.269). The most frequently encountered diltiazem-associated side effect was the occurrence of peripheral oedema (7 patients). Bronchospasm (n=1) and hypotension (n=4) were associated with β-blocker therapy. In rhythm-control group, six significant adverse effects were attributed to amiodarone, including symptomatic bradycardia (n=2), asymptomatic hypothyroidism (n=2), and symptomatic hyperthyroidism (n=1). All of 5 patients discontinued amiodarone, while 2 patients still remained in normal sinus rhythm and the other 3 patients relapsed to be crossed to rate control. Minor bleeding occurred in 8 patients (5 in rate-control group, 3 in rhythm-control group).

Hospital admissions
In rate-control group, 10 (11%) out of 91 patients were re-admitted to hospital at least once compared with 11 (12%) out of 92 rhythm-control patients (p=0.837). In rate-control group, the most frequent cause for hospital re-admission was drug-related side effects (70%). In rhythm-control group, most re-admissions were due to electrical cardioversion (64% of all hospital re-admissions). But rhythm-control strategy needed longer duration of hospital admission than rate-control strategy (13.17 ± 2.79 days vs. 7.71 ± 2.50 days, respectively; p=0.04). The main reason was amiodarone loading and electrical cardioversion in rhythm-control group.
DISCUSSION

To our best knowledge, this study is the first randomized trial to compare two different therapeutic strategies, rate versus rhythm control, in patients with AF after PMV. Our study demonstrated that during 12 months follow-up period, patients with AFD ≤ 12 months and post-PMV LA ≤ 45 mm, benefited from restoration and maintenance of sinus rhythm in terms of improvement in atrial-fibrillation-related symptoms, 6 min walking tests, QOL and LA normalization. Rhythm control should therefore be considered as the preferred initial therapy in this group of patients. This finding also may have important implications for patients with AF who have extensive comorbidity conditions and require symptom relief not provided by rate control.

Recent years, several randomized trials have compared heterogeneous groups of patients and the data are consistent and strong enough to promote a rate-control approach as the initial strategy for the vast majority of patients with persistent atrial fibrillation. Firstly, with current anti-arrhythmics a rhythm control approach does not lead to an improvement in symptom control or quality of life or a reduction in clinical events in the short to medium term. In the longer term, mortality may increase. Secondly, maintenance of sinus rhythm remains poor, even with an aggressive strategy combining electrical cardioversion and current anti-arrhythmics. Hence long-term therapeutic anticoagulation should be advocate for most patients treated with rhythm control, even if sinus rhythm is achieved in the short term. Thirdly, more admittance and adverse side effects remain a problem. But it should be pointed out that the above clinical trial samples consisted of elderly persons (mean age, ≥ 60 years), and mainly in non-valvular atrial fibrillation. Those data suggest that there was no benefit in attempting rhythm-control in these patients with a high risk of arrhythmia recurrence. It remains unclear whether the results in the rhythm-control group would have been better if sinus rhythm had been maintained in a higher proportion of patients.

Sinus rhythm is difficult to achieve and maintain in patients with rheumatic mitral valvular stenosis and AF, but would be more easily achieved with reduction of left atrial pressure after successful PMV. Our study confirms previous uncontrolled studies that indicated electrical cardioversion plus low-dose amiodarone is safe and effective in restoring and maintaining sinus rhythm in patients with AF after PMV. Our results show that 100% of patients were successfully cardioverted and 96% of patients could be maintained in sinus rhythm on continued low-dose amiodarone treatment over the observation period. This percentage was much higher than that in non-valvular fibrillation (PIAF, 56%). The reasons for the high efficacy observed in post-PMV patients are not entirely clear. Perhaps reduction of left atrial pressure after successful PMV induces sinus rhythm more easily to achieve and maintain. Among patients with shorter AFD and smaller LA, the post-PMV left atrial pressure is lower, thus sinus rhythm is easier to achieve and maintain. In our study, significant reductions of LA dimension were noted at one year compared with baseline, this indicated that reductions of LA dimension help to maintain sinus rhythm. On the other hand, only 2% patients in rate-control group were in sinus rhythm at one year. This percentage was lower than that in non-valvular fibrillation (PIAF, 10%). This result suggests that chronic AF after PMV is not associated with spontaneous reversion to sinus rhythm and measures should be undertaken to restore sinus rhythm. Low-dose amiodarone treatment was well
tolerated in this study. Serious toxicity necessitating discontinuation of therapy is infrequent. The actual crossover rate from rhythm control to rate control was 3.3% at 1 year, and this occurred primarily because of drug intolerance.

Our data suggest that results in the rhythm-control group would be better if sinus rhythm could maintain in a higher proportion of patients. One noted advantage is that symptomatic improvement is more easily achieved using rhythm-control strategy than rate-control strategy. Sinus rhythm was easily achieved after successful PMV, thus allowed for the good management of symptoms. Also, sustained sinus rhythm is associated with an improved quality of life and improved exercise performance. The study patients randomized to rhythm control had a better exercise tolerance compared with patients who underwent rate control. This finding may be due to improvement in haemodynamics after restoration of sinus rhythm. The improvement in atrial-fibrillation-related symptoms and exercise tolerance translated to an overall improved quality of life when both treatment groups were compared. These findings are in agreement with data from CRRAFT which was carried in patients with chronic rheumatic AF and 72.9% patients had undergone valvular interventions.

Successful PMV results in significant long-term reduction in LA size in most patients, but normalization of LA size is unusual. The outcomes of our trial revealed that the rhythm control strategy resulted in a partial reversal of LA remodeling, which has been found in other studies. Results of these studies may apply as powerfully to young patients, who have a longer risk for developing the potential complications of structural remodeling.

During the follow-up period, neither embolic nor transitory ischemic neurological events occurred, but it must mention that we cannot exclude the possibility that our sample size or time period was too small to detect significant differences in stroke rate between the two treatment strategies and the patients were young (aged 36.9 ± 5.4 years). Permanent anticoagulation may still be needed, although PMV may help prevent systemic embolism in patients with mitral stenosis. This issue requires further studies. Most of our patients were on aspirin therapy at baseline, which reflects common clinical practice in Mainland China.

The strategy of rhythm control was associated with similar times of hospital admissions in our patients, but longer duration of hospital stay. This meant higher medical cost. The higher cost for rhythm control confirms our intuition that this strategy often requires hospitalization for antiarrhythmic drug loading, cardioversion, or acute rate control for recurrent rapid atrial fibrillation. But rhythm control induces better clinical outcomes compared with rate control.

Is there still a place for rate control? It should be noted that patients with AFD > 12 months or post-PMV LA > 45 mm were excluded from our study. We were led to this decision by the high risk of AF recurrence of such patients. Therefore, rhythm control is not necessarily prior to rate control in those patients. In particular, rate control may be an acceptable alternative to rhythm control in patients who have a recurrence of AF after initial rhythm-control therapy. The treatment to AF should be individualized.

We compared rate control and rhythm control in patients with AF after PMV in a Chinese population composed of mostly young patients (mean age, 36.9 ± 5.4 years; range 25 - 56 years). Such findings are of interest in countries in which the incidence of rheumatic fever remains relatively high. The problem is different in the United States and
Europe, where patients with mitral stenosis and AF are older and more frequently have advanced heart disease. But our findings may provide an important aid in patient selection for rhythm control after PMV.

Patients with AF after PMV often need treatment for decades, even longer. The risk of relapse to AF or side effects with amiodarone therapy rises after 18 months. Furthermore, the use of amiodarone in young patients with normal ventricular function is something that cannot be justified. It has not yet been proven that prevention of atrial fibrillation will prolong survival. Therefore, whether rhythm-control treatment exerts long-term benefits on prognosis awaits further investigation.

In this study, the actual strategies themselves were not blinded, which created a potential bias. It is logistically and technically difficult if not impossible to blind therapies in this setting. Also, our sample was relatively small. This could have affected our results. Despite the limited number of patients, we detected significant differences between the two treatment strategies.

In conclusion, in patients with AF after PMV, AFD ≤ 12 months and post-PMV LA ≤ 45 mm, sinus rhythm could be easy and safe to achieve and maintain, moreover, patients benefited from restoration and maintenance of sinus rhythm in terms of improvement in atrial-fibrillation-related symptoms, 6 min walking tests, QOL and LA normalization. Rhythm control should therefore be considered as the preferred initial therapy in this group of patients. The optimal strategy to treat AF after PMV should be individualized.

Conflict of interest disclosures

We have no conflict of interests to disclose.

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**Figure 1.** Maintenance of sinus rhythm during the course of study.
**Figure 2.** Proportion of patients reporting improvement in clinical symptoms during follow-up. Rate control vs rhythm control at any point, $p < 0.0001$, respectively.
Figure 3. Mean data in exercise tolerance as assessed by repeated 6 min walk tests. Error bars show 95% CI.