Percutaneous transvenous mitral commissurotomy (PTMC) is an effective treatment in patients with symptomatic mitral stenosis (MS) and a favorable valve anatomy.1–5 Atrial fibrillation (AF) is often associated with symptomatic MS, and the restoration and maintenance of sinus rhythm (SR) can be difficult using antiarrhythmic drugs, even after PTMC.6–9 Radiofrequency catheter ablation (RFCA) for the suppression of premature atrial contraction (PACs), triggering AF within the pulmonary veins (PVs), has been developed as a curative therapy in patients with symptomatic drug-resistant AF.10–12 In initial studies, radiofrequency (RF) energy was applied to the focus of the PAC within the PV that triggered the AF (focal ablation), but recently, segmental electrical isolation of the PVs (PV isolation) has been performed in patients with AF.13–16 However, few studies have examined the utility and safety of performing RFCA and PTMC simultaneously in patients with MS and AF.17 The purpose of this study was to clarify the efficacy and safety of RFCA following PTMC in patients with MS and AF.

Methods

Study Population

Between February 2000 and October 2003, RFCA for AF was performed following PTMC in 4 patients with MS and drug-resistant AF (2 men, 2 women; mean age (range), 59±6 (52–63 years); 2 cases of paroxysmal AF, 2 of persistent AF; Table 1). The duration of AF was 3.4±3.3 years (range, 0.5–8.0 years). AF had persisted for 3 months in patient 4, and >2 months in patient 3. Patients 1 and 4 had a history of a failed electrical cardioversion for AF. The mean number of antiarrhythmic drugs that had been ineffective in preventing recurrences of AF before the ablation procedure was 3.3±1.3. All patients had MS that was amenable to PTMC. Echocardiography demonstrated a mean left ventricular ejection fraction of 0.58±0.04 and a mean left atrial diameter (LAD) of 47±7 mm. The mean mitral valve area (MVA) was 1.11±0.19 cm², and there was no or grade I mitral regurgitation (MR), determined by left ventriculography before the procedure (Table 2).18–21

PTMC

After informed consent was given, PTMC was performed as previously described.1–4 Right femoral venous access was obtained and the transseptal approach with an Inoue balloon was used in all patients. The initial balloon size was determined just before each commissurotomy procedure. The balloon size was increased stepwise until a MVA of more than 1.7 cm² was reached or MR increased to more severe.
than grade 2/4. The severity of the MR was evaluated by left ventriculography. The MVA was measured by 2-dimensional echocardiography. The mitral orifice was visualized using the parasternal short axis view and its area was determined by manual planimetry. Measurements were repeated 3 times for the different cardiac cycles and the mean value was used for analysis. Echocardiographic examination was scheduled in the follow-up period.

Electrophysiologic Study and RCA

Electrical cardioversion was performed at the end of the PTMC in 3 patients when they demonstrated AF. PV isolation was performed in 3 patients (patients 2, 3, 4), and focal ablation was performed in the remaining patient (patient 1). RFCA was performed for the arrhythmogenic PVs. An arrhythmogenic PV was defined as a PV in which a PAC triggering AF was identified during SR and/or as a PV demonstrating PV tachycardia during AF. Segmental isolation was attempted in each of the 3 patients as previously described. A 7Fr decapolar ring catheter (Lasso, Biosense Webster, Diamond Bar, CA, USA) and a 7Fr quadripolar ablation catheter with a 4-mm distal electrode, embedded thermistor, 2–5 mm inter-electrode spacing, and a deflectable tip (Biosense Webster) were inserted into the left atrium. In all cases, mapping and catheter ablation were performed during SR or coronary sinus pacing. Selective PV angiograms were performed to identify the PV ostia. The Lasso catheter was positioned inside the PV, within 5 mm of the ostium. Target sites for ablation were selected by identifying the PV potentials that had an equivalent or earlier activation relative to the adjacent Lasso catheter recording sites. The ablation catheter was always positioned in close proximity and on the ostial side of the Lasso catheter.

Focal ablation within the PV was performed in the remaining patient (patient 4). After mapping for the PAC that was triggering the AF, RF energy was applied at the site where the earliest atrial activation during a PAC was recorded within the PV. RFCA was performed using a maximum power of 30 W and a maximum electrode-tissue interface temperature of 52–55°C. The applications of energy were 60–120 s in duration. The end-point for ablation was the elimination of the PV potentials at all Lasso catheter recording sites. After the procedure, heparinization was continued to maintain a partial thromboplastin time between 70 and 90 s. Antiarrhythmic drugs were discontinued at least 48 h before the procedure and restarted for the follow-up period in all patients. Narrowing of the PVs was determined by computed tomography 2–6 months after the ablation procedure.

Clinical Follow-up

Patients were followed-up after the procedure for 32 ± 20 months (range, 6–54 months). To confirm the absence of AF, a 12-lead ECG was recorded on each visit to the clinic, and 24-h Holter monitoring also was performed at least once during the follow-up period. Recurrence of AF was defined as recurrence of symptoms suggestive of tachycardia and an episode of AF documented on the 12-lead ECG or 24-h Holter monitor during the follow-up period. Clinical events during the follow-up were defined as the need for mitral valve replacement (MVR), worsening of congestive heart failure (CHF) requiring hospitalization, or onset of thromboembolism.

Statistical Analysis

Continuous variables are expressed as the mean ± standard deviation, and were compared using the Student’s t-test. A p-value < 0.05 was considered statistically significant.

Results

Acute Results of PTMC and RFCA

After the PTMC, MVA increased from 1.11 ± 0.19 cm² to 1.90 ± 0.20 cm² (p < 0.01), and the mean left atrial pressure decreased from 15.5 ± 4.3 mmHg to 4.5 ± 2.5 mmHg (p < 0.05) (Table 2). No worsening of MR occurred immediately after the PTMC in any of the patients. Electrical isolation was achieved in 6 of 6 PVs in 3 patients (patients 2, 3, 4; Table 3). In the remaining patient (patient 1), the origin of the PAC triggering AF was successfully eliminated within

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (years)</th>
<th>Gender</th>
<th>NYHA</th>
<th>Type of AF</th>
<th>AF history (years)</th>
<th>AF duration (months)</th>
<th>LAD (mm)</th>
<th>EF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>52</td>
<td>F</td>
<td>II</td>
<td>Paroxysmal</td>
<td>3</td>
<td>–</td>
<td>55</td>
<td>61</td>
</tr>
<tr>
<td>2</td>
<td>64</td>
<td>M</td>
<td>II</td>
<td>Paroxysmal</td>
<td>2</td>
<td>–</td>
<td>43</td>
<td>62</td>
</tr>
<tr>
<td>3</td>
<td>58</td>
<td>M</td>
<td>II</td>
<td>Persistent</td>
<td>Unknown</td>
<td>&gt;2</td>
<td>40</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>63</td>
<td>F</td>
<td>II</td>
<td>Persistent</td>
<td>8</td>
<td>3</td>
<td>51</td>
<td>54</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; NYHA, New York Heart Association functional class; LAD, left atrial dimension; EF, ejection fraction.
the left superior PV (Table 3). The number of RF energy applications per patient was 15.0±9.1 and the mean RF duration was 22.5±11.6 min. The mean duration of the entire procedure was 227.0±24.6 min, and the fluoroscopy time was 109.8±14.4 min. No complications, such as a pericardial effusion or femoral hematoma, occurred in any of the patients.

Recurrence of MS and AF

The MVA was 1.83±0.29 cm² at the end of the follow-up period, and mitral valve (MV) restenosis did not occur during the follow-up period (Table 4). The LAD decreased slightly to 46±8 mm (p=0.34). All patients were treated with antiarrhythmic drugs after the procedure (pilsicainide in 2 patients; amiodarone in 2 patients). In 1 patient (patient 4), AF recurred 10 days after the procedure and SR could not be maintained. However, SR was retained in the other patients (patients 1, 2, 3). Two had no symptomatic AF attacks during the follow-up period, but 1 still had episodes of paroxysmal AF during the follow-up period. No cardiac deaths, MVR, CHF, thromboembolism, or PV stenosis >50% was observed during the follow-up period.

Discussion

Major Findings

The results of this study demonstrated that the combined therapy of PTMC and RFCA is feasible and moderately effective in patients with MS and AF. After the PTMC, RFCA was performed with no complications, and SR was restored or the AF episodes disappeared or were decreased dramatically after this procedure. Although SR could not be maintained in 1 patient, a favorable outcome was still achieved with this approach and the clinical status improved in the other 3 patients. Therefore, we believe that this approach should be considered for the treatment of patients with MS and drug-resistant AF.

Benefits of RFCA Following PTMC in Patients With MS

It is well known that AF is frequently associated with MS, and that AF is an unfavorable factor for the long-term prognosis. PTMC has become an alternative therapy to surgical mitral commissurotomy in patients with MS, and survival without the need for mitral surgery has been reported as 84% and the prevention of combined cardiac events (death, mitral surgery, and New York Heart Association class III or IV heart failure) as 76% through 32±8 months of follow-up in 528 post-PTMC patients. After PTMC, an acute reduction in the chronic atrial stretch in patients with MS results in favorable effects on the atrial electrophysiologic characteristics, which may be effective in the restoration of SR or reduction of AF episodes. However, PTMC alone is insufficient for maintaining SR in patients with AF and MS. Kathle reported that of 54 patients with chronic AF before PTMC who underwent successful electrical cardioversion and received amiodarone, only 26 patients (49%) remained in SR after 18 months. Langerveld et al also reported that in 11 patients with chronic AF before PTMC who underwent successful electrical cardioversion, only 4 patients (36%) remained in SR after 4 years.

Several studies have reported that epicardial RF ablation or cryoablation of the PVs and/or left atrium following MVR was effective for restoration of SR in patients with MS. Therefore, we consider that RFCA of the PVs and PTMC might become an alternative to surgical treatment. RFCA is performed worldwide in patients with MS and PV isolation is an effective treatment for patients with paroxysmal AF. Focal ablation at the origin of the PAC triggering the AF is also effective when the triggered PAC can be mapped precisely during the ablation procedure. PV isolation has been reported to be less effective for patients with chronic AF, because the contribution of the PVs in the setting of chronic AF may be much less than in paroxysmal AF. However, recent studies demonstrate that the posterior left atrium, including the PVs, plays an important role in the genesis and maintenance of AF in patients

Table 3 Acute Results of Radiofrequency Catheter Ablation (RFCA)

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>RFCA strategy</th>
<th>No. of targeted PVs</th>
<th>Targeted PVs</th>
<th>Result</th>
<th>No. of RF applications (PV)</th>
<th>Duration of RF energy (min/PV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Focal</td>
<td>1</td>
<td>LS</td>
<td>Success</td>
<td>7.0</td>
<td>9.2</td>
</tr>
<tr>
<td>2</td>
<td>Isolation</td>
<td>3</td>
<td>LS, LI, RS</td>
<td>Success</td>
<td>9.0</td>
<td>10.7</td>
</tr>
<tr>
<td>3</td>
<td>Isolation</td>
<td>1</td>
<td>LS</td>
<td>Success</td>
<td>9.0</td>
<td>13.0</td>
</tr>
<tr>
<td>4</td>
<td>Isolation</td>
<td>2</td>
<td>LS, LI</td>
<td>Success</td>
<td>11.5</td>
<td>16.5</td>
</tr>
</tbody>
</table>

PV, pulmonary vein; LS, left superior pulmonary vein; LI, left inferior pulmonary vein; RS, right superior pulmonary vein.

Table 4 Follow-up Results

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Duration (months)</th>
<th>NYHA</th>
<th>MVA (cm²)</th>
<th>LAD (mm)</th>
<th>EF (%)</th>
<th>No. of AF episodes</th>
<th>AADs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53.7</td>
<td>1</td>
<td>1.8</td>
<td>53</td>
<td>61</td>
<td>None</td>
<td>Pilsicainide</td>
</tr>
<tr>
<td>2</td>
<td>30.7</td>
<td>1</td>
<td>1.5</td>
<td>37</td>
<td>62</td>
<td>3 times/2 years</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>3</td>
<td>39.4</td>
<td>1</td>
<td>2.2</td>
<td>40</td>
<td>73</td>
<td>None</td>
<td>Pilsicainide</td>
</tr>
<tr>
<td>4</td>
<td>5.3</td>
<td>1</td>
<td>1.8</td>
<td>52</td>
<td>61</td>
<td>CAF</td>
<td>Amiodarone</td>
</tr>
</tbody>
</table>

NYHA, New York Heart Association functional class; MVA, mitral valve area; LAD, left atrial diameter; EF, ejection fraction; AF, atrial fibrillation; AADs, antiarrhythmic drugs; CAF, chronic atrial fibrillation.
with chronic AF\textsuperscript{3} In fact, cryoablation at the PV ostia, including the posterior wall of the left atrium following MVR, has demonstrated favorable outcomes in the restoration and maintenance of SR\textsuperscript{27–30} The Cox maze procedure with MVR or repair has been established as a surgical method for patients with MV disease and AF, and the freedom from the AF at 5 years after this combined approach is approximately 80\%\textsuperscript{31} Therefore, although this surgical treatment is more invasive for the patient than the combined treatment of RFCA and PTMC, it might be better than RFCA and PTMC for restoring and maintaining SR in patients with MS and AF. However, MVR is associated with a higher hospital and late mortality than PTMC, and there are complications related to the prosthesis! Mitral valve repair may be as effective and safe as PTMC; however, the appropriate skill and experience are required for this technique! The success rate of PTMC is \textgreater\textgreater95\%, and the hospital stay after PTMC may be shorter than that after MV replacement or repair. Although the number of patients studied in the present study was small, we were able to perform this combined approach with no complications. As a result, all patients, except one, who had a dilated left atrium and long-standing history of AF maintained SR and had either disappearance or significant reduction in the AF episodes. Therefore, we believe that this combination should be considered when the patient has MS and AF. Furthermore, although a moderate MS (MVA of 1.0–1.5 cm\textsuperscript{2}) does not serve as an indication of PTMC in MS and AF. Therefore, although a moderate MS (MVA this combination should be considered when the patient has MS and AF. However, many cases, patients with moderate MS, suffering from drug-resistant AF, may be suitable candidates. However, when the patient is not a good candidate for PTMC (ie, a rigid MV, presence of severe MR or left atrial thrombi, or the need for other cardiac surgeries), the maze procedure with MV surgery should be selected as the first-line therapy for the patients with MS and AF\textsuperscript{5}.

**Previous Studies**

As mentioned before, several studies have reported on the utility of ablation therapy for AF after MVR\textsuperscript{27–30} However, only 1 study, by Adragao et al, examined the utility of RFCA following PTMC and they reported that of 5 patients with MS and AF (age 43±4 years; chronic AF in all of the patients diagnosed 31±12 months previously) who underwent PTMC and concomitant PV isolation, 3 maintained SR after 5 years\textsuperscript{37}.

**Study Limitations**

First, segmental PV isolation or focal ablation was performed as the RFCA method for AF in the present study. However, an empiric 4 PV isolation or wide area circumferential ablation in the left atrium has recently been reported as a more effective treatment for AF\textsuperscript{32,33} Therefore, a combined approach of PTMC and those new ablation methods might have resulted in a more favorable outcome in restoring and maintaining SR.

Second, our sample size was small and the follow-up period after the procedure was relatively short, which might obscure the effectiveness and safety of the RFCA and PTMC in patients with MS and AF. Therefore, future studies that include a larger number of patients may be needed to clarify the role of this combined treatment.

**Conclusion**

RFCA for AF following PTMC is safe and feasible, and may be effective in restoring SR or suppressing AF episodes in patients with MS and drug-resistant AF.

**Acknowledgments**

This work was supported by a research grant for Cardiovascular Diseases (14C-2) from the Ministry of Health, Labor and Welfare, Japan. We are indebted to Ms Rika Utsugi and Mr Tsutomu Nakajima for their important contributions to this study.

**References**

19. Wissenburg T, Berk M, Essen R, Middelstorp S, Sarel P. Effect of mitral regurgitation and volume loading on pressure half-time before


