Chronic Atrial Fibrillation in Patients With Rheumatic Heart Disease

Mapping and Radiofrequency Ablation of Flutter Circuits Seen at Initiation After Cardioversion

Mohan Nair, MD; Prasad Shah, MD; Ravinder Batra, MD; Manoj Kumar, MD; Jagdish Mohan, MD; Upkar Kaul, MD; Ramesh Arora, MD

Background—There is little information concerning mapping and radiofrequency ablation (RFA) of arrhythmias seen during reinduction of atrial fibrillation (AF) after pharmacological and/or electrical cardioversion in patients with chronic AF and rheumatic heart disease.

Methods and Results—Seventeen patients with rheumatic heart disease and symptomatic chronic AF underwent multisite atrial mapping during reinduction of AF after cardioversion. An organized atrial arrhythmia of varying duration was seen to precede the AF in all patients. The earliest atrial activity during this organized rhythm was near the coronary sinus ostium (CS OS) in 14 patients and along the left side of the interatrial septum (IAS) in 3 patients. RFA was performed in 16 patients (14 near the CS OS and 2 along the IAS). Postablation AF was inducible in 1 patient in whom RFA was performed near the CS OS and in both patients when it was performed along the IAS. At a follow-up of 6 to 56 weeks (mean, 32 weeks), 10 of the 13 patients who had successful ablation were in sinus rhythm. All patients in whom AF was inducible immediately after RFA continue to be in AF.

Conclusions—Induced AF in patients with rheumatic heart disease begins as a rapid organized arrhythmia with earliest atrial activity near the CS OS in most patients. RFA targeting the region of the CS OS is successful in suppressing the arrhythmia immediately in most of the patients and in most on follow-up. (Circulation. 2001;104:802-809.)

Key Words: atrial fibrillation ■ rheumatic heart disease ■ ablation

Atrial fibrillation (AF) is the most common sustained arrhythmia, being present in 0.4% of the overall population and in 3% to 5% of those >65 years of age. This incidence is higher in countries with a high prevalence of rheumatic heart disease (RHD). In these countries, AF contributes to significant morbidity and mortality in a relatively young population. Limitations associated with drug treatment in maintaining sinus rhythm in patients with AF have sped the search for nonpharmacological therapies, including investigation of ablation procedures. Definitive catheter ablation procedures for AF are not yet well established.

Work on ablation of AF has so far been done mostly in patients who have paroxysmal AF and a normal heart. There are few data on mapping and catheter ablation for chronic AF in patients with structural heart disease. The objectives of this study were to conduct multisite mapping and to attempt ablation of atrial arrhythmias seen during reinduction of AF after pharmacological or electrical cardioversion in patients with RHD and chronic AF.

Methods

Study Population

The study population consisted of 17 patients (8 men and 9 women; mean age, 30.6 years; range, 22 to 45 years) with RHD and symptomatic chronic AF. All patients had undergone a successful balloon mitral valvotomy ≥4 weeks before the study. The mean mitral valve area was 1.5 cm², and the mean left atrial diameter was 5.3 cm (range, 3.6 to 6.2 cm). The duration of AF was 7±1.2 years.

Preprocedure Evaluation and Drug Therapy

Patients received oral amiodarone 400 mg twice a day for 10 days and were started on 5000 U heparin IV every 6 hours, which was continued up to 6 hours before the study. An echocardiographic examination (transthoracic and transesophageal) was done 1 day before the procedure to rule out any clot in the atria and to assess chamber size and mitral valve area.

Electrophysiological Study

The study was done in patients in a fasting state under local anesthesia after written informed consent was obtained. The institutional review committee approved the study protocol.
amiodarone because these patients had a left atrium in 8 patients; 5 patients with significant mitral regurgitation were on oral anticoagulants, which they were advised to continue for 3 months. All patients who had successful ablation were discharged and were followed up every 15 days for the first 3 months and then once daily on the second and third day. Patients had continuous rhythm monitoring in the intensive care unit for 24 hours, and ECGs were taken every 6 hours for the first 24 hours and once daily on the second and third day. Postprocedure Protocol

Low-molecular-weight heparin 5000 U SC was given twice a day for 3 days. Patients had continuous rhythm monitoring in the intensive care unit for 24 hours, and ECGs were taken every 6 hours for the first 24 hours and once daily on the second and third day. Patients were followed up every 15 days for the first 3 months and then monthly. All patients who had successful ablation were discharged on oral anticoagulants, which they were advised to continue for 3 months. Antiarrhythmic drugs, including amiodarone, were stopped in 8 patients; 5 patients with significant mitral regurgitation were continued on amiodarone because these patients had a left atrium 6 cm². Antiarrhythmic drugs were continued in patients in whom radiofrequency ablation (RFA) was considered unsuccessful.

Results

Electrophysiological Study
Sustained AF was reproducibly induced in all patients. Induction was by atrial extra stimuli in 7 (right atrium in 4, CS in 3) and by rapid atrial pacing in 10 (right atrium in 7, CS in 3) patients. There was no difference in induced arrhythmias in patients who converted spontaneously on amiodarone and those who required additional DC cardioversion to restore sinus rhythm. Induced AF in each patient was preceded by an organized atrial arrhythmia that could be clearly mapped (Figure 2A and 2B). The cycle length of the initial arrhythmia ranged from 260 to 350 ms. Intracardiac mapping at the onset of induced AF showed earliest atrial activity (as gauged from the onset of the P wave in lead V1) to be in the region of the CS ostium (CS OS) in 14 patients and along the left side of the IAS in 3 patients. Entrainment during this tachycardia was attempted in 5 patients (2 at the IAS and 3 at the CS OS). Concealed entrainment was achieved in 3 patients (Figure 3), and in the other 2, attempts at entrainment failed because of degeneration of the rhythm at the start of each pacing attempt. In the rest, the atrial arrhythmia terminated or degenerated into AF before entrainment could be attempted. A surface electrogram recorded at the time of organized atrial activity was classified as atypical flutter in all patients (Figure 4). The arrhythmia was considered to be organized when endocardial electrograms showed well-defined, stable atrial electrograms in all the mapped regions. The atrial electrograms were separated by an isoelectric line, and the cycle length was stable. Atypical flutter was defined as an atrial arrhythmia with an ECG pattern of continuous undulation of atrial complex in ≥1 lead, and flutter-wave morphology was different from typical flutter. The organized atrial rhythm lasted for various lengths of time in each patient (5 to 45 minutes). It then showed destabilization, first showing switching of activation pattern and cycle length variations within the CS before degenerating into AF (Figure 5).

Spontaneous Ectopic Activity
Spontaneous ectopic beats were seen in 3 patients after cardioversion. In each patient, the earliest atrial activity during these beats was seen at the CS OS. In no patient was spontaneous reinitiation of AF seen during a waiting period of up to 30 minutes.

Pulmonary Vein Electrical Activity
Mapping of the 2 superior pulmonary veins or 1 superior and 1 inferior pulmonary vein was done during the entire procedure in 5 patients. In no patient was any electrical activity detected within the pulmonary veins during either sinus rhythm or atrial flutter/AF (Figure 5).

Radiofrequency Catheter Ablation
RFA was attempted in 16 patients showing earliest activity during organized atrial rhythm at the CS OS (14 patients) or the IAS (2 patients). The target site chosen for ablation was the one that during atypical flutter showed the following...
features: earliest atrial activation, fractionated atrial electrogram, and/or concealed entrainment. The region near CS OS straddling its superior or inferior rim was the site of earliest atrial activation during the tachycardia in most patients. This was independent of the pacing site at induction or the rate/coupling interval on induction of AF. Radiofrequency energy was delivered during ongoing atrial arrhythmia in 8 patients and during sinus rhythm after mapping during short...
Figure 3. A. Entrainment of induced atrial flutter from CS OS. Activation sequence during spontaneous rhythm and pacing are identical.
B. After pacing, flutter cycle length remains stable and does not degenerate into AF.
runs of atypical flutter in 9 patients. When ablation was performed in sinus rhythm, reinduction was attempted after each RF pulse.

Results of Ablation
A total of 2 to 6 pulses (mean, 3.6) were delivered.

Patients With Earliest Activation Near the CS OS
Energy was delivered during sinus rhythm in 7 patients and during ongoing atrial arrhythmia in 7 patients. Sinus rhythm was restored in 7 patients in whom the energy was delivered during the ongoing atrial arrhythmia (Figure 6). After ablation, AF was not inducible in 13 patients.

Patients With Earliest Atrial Activity at the IAS
We were unsuccessful in terminating the tachycardia in 2 patients in whom ablation was performed along the IAS. Ablation was not attempted in 1 patient in whom the earliest site of activation was at the IAS because the tachycardia was entrainable over a large area. Ablation was considered successful when there was termination of the atrial flutter during delivery of the RF pulse and/or neither atypical flutter nor sustained AF was inducible. With these criteria, 13 of 14 patients with flutter mapped to the CS OS and none of the patients with flutter mapped to the IAS were considered to have an acute success.

Follow-Up
At a follow-up ranging from 6 to 56 weeks (mean, 32 weeks), 10 of the 13 patients who had an initial successful ablation were in sinus rhythm, whereas 3 patients have had a recurrence of AF. Among these, 3 patients were on amiodarone therapy. Those patients in whom the initial ablation was unsuccessful or not attempted continued to be in AF. A summary of findings during electrophysiology, ablation, and follow-up is given in the Table.

Discussion
Salient Findings
In this study conducted in patients with chronic rheumatic AF, we have observed that at reinduction there is an organized atrial tachycardia preceding the onset of AF. These arrhythmias can be clearly mapped, and the earliest site of atrial activation is often at the CS. It was seen that it is possible to ablate the tachycardias seen to originate in the region of the CS OS, with attendant suppression of AF inducibility in the acute phase.

Different Patient Population, Different Mechanism
The fact that at least some subgroups of AF may be amenable to “cure” by radiofrequency catheter ablation has become increasingly evident in recent years. The most widely
studied have been those with paroxysmal AF who have a rapidly firing focal source, usually in 1 of the pulmonary veins. Ablation of this focal source has led to cure of AF in many of these patients.7,9,12–14 We have not found areas of focal discharges but atypical flutter circuits anchoring around specific anatomic sites (CS OS and IAS). Potentially diverse electrophysiological mechanisms and substrates exist in different patient populations. Valvular heart disease, particularly mitral valve disease, results in increased atrial chamber pressures, atrial stretch, increased atrial size, atrial muscle disruption, and fibrosis.15 Myocardial stretch has been demonstrated to slow conduction velocity, shorten refractory periods, increase the dispersion of refractoriness, and stimulate ectopic excitation, all influences that promote sustained intra-atrial reentry and fibrillation.16 These patients have sufficient electrophysiological substrate to initiate and main-

Figure 5. Presence of switching of activation pattern and variation in cycle length of organized atrial rhythm that was typically seen before degeneration into AF. Earliest site of atrial activation is seen to move from CS 9,10 to CS 7,8 in 6th and 7th beats (arrows). Atrial activation is earliest in CS 7,8 in 9th beat. Atrial activation then switches back to being earliest in CS 9,10 in 10th beat. There is also evidence of cycle length variation between 6th and 7th beats (240 ms) and 9th and 10th beats (300 ms). PV 1 through 8 represent pulmonary vein ECGs. Note absence of any electrical activity in pulmonary veins.

Figure 6. Restoration of sinus rhythm when RFA is being performed during ongoing AF.
tain AF, even in the absence of pulmonary vein ectopics. It is likely that rapid atrial arrhythmias anchoring around anatomical orifices degenerate into AF in this patient population. This is in agreement with the hypothesis suggested by Konings et al\textsuperscript{10} that although the atria as a whole participate in the process of AF, not all the parts of the atria contribute equally to the perpetuation of the fibrillatory process. Our findings are potentially applicable to the largest group of patients with AF resulting from RHD.

**Mapping of AF in Patients With Structural Heart Disease**

Saksena et al\textsuperscript{18} performed simultaneous catheter mapping of left and right atrial regions at onset and sustenance of spontaneous and induced AF in patients with ischemic and/or hypertensive heart disease. Although the disease state affected the structure of the left side of the heart mechanically and hemodynamically, right atrial origin of premature complexes or onset cycles of spontaneous AF was seen. Both spontaneous and induced AF began as rapid organized atrial arrhythmia, with earliest activation on right side, before degenerating into AF. Our findings are similar to those of Saksena et al.\textsuperscript{18} We also found organized atrial arrhythmias at initiation on induction that degenerated into AF after a variable duration. However, the region of earliest activation was found to be the CS OS in most patients. Our study population was different in that all patients had RHD and chronic AF. Moreover, the patients were on amiodarone at the time of the study. This could also explain the relatively stable atrial arrhythmias we induced that allowed mapping and ablation.

**Importance of the CS**

In one of the earliest reports on the surgical maze procedure, Cox et al\textsuperscript{19} clearly recognized the importance of disconnection of the fibers around the CS as the most important step in the surgical cure of AF. Chauvin et al\textsuperscript{20} have demonstrated histologic continuity between the right atrium and left atrium through the CS myocardium in humans. These connections are made of striated muscle fibers arranged in 2 distinct parts: a muscular cuff surrounds the CS wall along 25 to 51 mm of its length, and other fibers emerge from this cuff to join the left atrial myocardium. These fibers have anatomic characteristics varying from a few discrete fascicles to a wide interconnection plexus. Antz et al\textsuperscript{21} have confirmed the existence of CS–left atrial connections. They probably reflect the embryological development of this part of the heart where in a narrow band around the mitral annulus is formed from the primitive atrium that retains the muscular interconnection. This interatrial connection through the CS may explain our findings of the earliest atrial activity during reinduction near the CS OS and the success in suppressing the arrhythmia immediately in all the patients near the CS OS and in most patients on follow-up. Olgin et al\textsuperscript{22} have also described atrial macroreentry involving the myocardium of the CS as a mechanism for atypical flutter and the success achieved in ablating this arrhythmia by circumferential radiofrequency application within the CS.

Important differences between our study and most other studies reporting a focal initiating or triggering arrhythmia in AF are the absence of spontaneous initiation of AF by focal firing, especially from the pulmonary veins, and the absence of any spontaneous or induced electrical activity in the pulmonary veins. The absence of spontaneous initiation by ectopic foci may have been due to the fact that all patients in this study were on amiodarone. The absence of pulmonary vein electrical activity is not readily explained. It may be postulated that chronic RHD may have caused fibrous replacement of the myocardial extension into the pulmonary veins; in addition, the amiodarone used by all our patients could have suppressed the electrical activity.

The impact of ablation of these reentry circuits seen at induction of AF on long-term maintenance of sinus rhythm has not been studied so far. In our study, we have clearly shown that (1) these initiating arrhythmias can be mapped and ablation performed; (2) after ablation, the acute inducibility of AF is suppressed; and (3) most patients who have had these arrhythmias ablated have maintained sinus rhythm on follow-up. It may therefore be safe to assume that these atypical flutter circuits seem to have a certain role in the initiation and maintenance of chronic AF. The number of patients studied, however, does not allow us to comment on whether arrhythmias anchoring around anatomic structures other than the CS OS and IAS play a role in chronic AF.

**Summary of Findings**

<table>
<thead>
<tr>
<th>Earliest Atrial Activation</th>
<th>Patients, n</th>
<th>RFA Attempted, n</th>
<th>AF Termination During RFA, n</th>
<th>AF After RFA, n</th>
<th>Presence of AF on Follow-Up, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left atrium</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IAS</td>
<td>3</td>
<td>2/3</td>
<td>0</td>
<td>2/2</td>
<td>3/3 (100)</td>
</tr>
<tr>
<td>CS OS</td>
<td>14</td>
<td>All</td>
<td>7</td>
<td>1/14</td>
<td>4/14 (23.52)</td>
</tr>
</tbody>
</table>

**Study Limitations**

This study has several limitations. First, more high-density mapping and anatomic correlation is necessary to better define the flutter circuit and its relationship to the CS OS. Second, the studied patients were post–percutaneous transvenous mitral commissurotomy and on amiodarone. This prevented spontaneous recurrences of AF during mapping. Improved hemodynamics after percutaneous transvenous mitral commissurotomy could have contributed to our success. Absence of a control group of patients not on amiodarone and without balloon mitral valvotomy is an important limitation of our study. However, amiodarone was given to this patient population to ensure successful cardioversion and to minimize shocks during external cardioversion. Amiodarone also helps in organizing atrial activity at the time of induction. The
resulting induced arrhythmias showed organized atrial activity and were stable for sufficient duration to allow mapping. Third, induced and not spontaneous arrhythmias triggering AF were targeted for ablation. Although targeting the induced arrhythmias resulted in acute success, amiodarone might have suppressed other potential atrial arrhythmia circuits that can lead to AF at follow-up. Finally, a larger number of patients with a longer follow-up is required to give more power to the clinical implications of our findings.

Conclusions
Induced AF seen after cardioversion of chronic AF in patients with RHD begins as a rapid organized arrhythmia. The region near the CS OS is the site of the earliest atrial activation during initiation in most patients, and this is independent of the stimulation site. RFA targeting the region of the CS OS is successful in suppressing the arrhythmia immediately in most of the patients and in most on follow-up.

References
Chronic Atrial Fibrillation in Patients With Rheumatic Heart Disease: Mapping and Radiofrequency Ablation of Flutter Circuits Seen at Initiation After Cardioversion
Mohan Nair, Prasad Shah, Ravinder Batra, Manoj Kumar, Jagdish Mohan, Upkar Kaul and Ramesh Arora

_Circulation_. 2001;104:802-809
doi: 10.1161/hc3201.094228
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/104/7/802

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/