Effects of Cavotricuspid Isthmus Catheter Ablation on Paroxysmal Atrial Fibrillation

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SUMMARY

It has been demonstrated that successful cavotricuspid isthmus ablation of typical atrial flutter combined with atrial fibrillation (AF) sometimes influences the preablation history of paroxysmal AF. However, the effectiveness of only isthmus ablation on AF itself is unclear.

Endocardial catheter mapping during induced AF was performed around the tricuspid annulus using duodecapolar electrode catheters in 39 patients with drug-refractory paroxysmal AF. Isthmus ablation was performed in 16 patients (41%) in whom catheter mapping during AF showed an organized activation pattern around the tricuspid annulus.

During a mean follow-up of 12.3 months, isthmus ablation was successful in preventing AF in 12 (75%) patients, 8 without medication and 4 with a previously ineffective drug. This success group had a significantly higher F wave amplitude in lead V1 (0.29 ± 0.10 vs 0.15 ± 0.04 mV, \( p < 0.01 \)), a higher left ventricular ejection fraction (74 ± 9 vs 58 ± 2%, \( p < 0.05 \)), and a smaller left atrial dimension (35 ± 6 vs 43 ± 4mm, \( p < 0.05 \)) than the failure group.

Isthmus ablation may be effective in preventing paroxysmal AF with an organized activation pattern around the tricuspid annulus. F wave amplitude, left ventricular ejection fraction, and left atrial dimension were significant predictors of success. (Jpn Heart J 2001; 42: 79-89)

Key words: Atrium, Fibrillation, Catheter ablation, Mapping

Previous catheter ablation techniques\(^1\)-\(^9\) to prevent or cure atrial fibrillation (AF) have required the placement of numerous and extensive lesions in both atria. In contrast, Gaita, et al.\(^{10}\) performed catheter ablation only in the right atrium, and suggested that a limited but effective ablation to prevent or cure AF may be possible in some patients with idiopathic AF. Moreover, it has been demonstrated that successful cavotricuspid isthmus ablation of typical atrial flutter combined with AF\(^{11,12}\) or flutter converted from AF by antiarrhythmic drugs\(^{13}\)

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sometimes influences the preablation history of paroxysmal AF. However, the effectiveness of only isthmus ablation on AF itself is unclear.

The Maze operation and catheter Maze ablation are largely based on the multiple reentrant wavelet hypothesis.\(^{14-17}\) In contrast, mapping studies of AF in the canine sterile pericarditis model have shown that AF is generated by multiple unstable reentrant circuits.\(^{18}\) In this model, ablation cured AF by making a linear lesion at a single location to prevent the continued formation of mother reentrant circuits which were identified by their organized activation pattern. Therefore, we hypothesized that an organized activation pattern around the tricuspid annulus during AF indicated a mother reentrant circuit that could be terminated by a cavocaval isthmus ablation, thus preventing AF. The objectives of the present study were to evaluate the effectiveness of isthmus ablation in preventing AF and to identify predictors of its success.

**METHODS**

**Study population:** The study population consisted of 39 patients (23 men and 16 women; mean age 63 ± 18 years) referred for symptomatic drug-refractory (number of drugs, 3 ± 1) paroxysmal AF with daily to weekly sustained episodes. In all patients, an analysis of available 12-lead ECGs showed tracings typical of sustained AF. Patients without inducible AF during an electrophysiologic study were excluded from this study. Informed consent was obtained from all patients before the study.

**Electrophysiological study:** Antiarrhythmic drugs were discontinued for at least five half-lives. One Halo catheter (Cordis Webster) with 20 electrodes was positioned in the right atrium to map around the tricuspid annulus. A duodecapolar catheter (Cordis Webster) was positioned in the right atrial appendage for incremental or programmed atrial stimulation. A decapolar catheter (Daig Corp) was inserted into the distal coronary sinus to map the region of the lateral wall of the left atrium adjacent to it. Bipolar intracardiac electrograms were recorded at a filter setting of 30 to 500 Hz and stored digitally on an EPLab system (Quinton Electrophysiology, Inc.) simultaneously with the surface ECG. Stimuli were twice the diastolic threshold and 2 ms long. If AF was not spontaneously present, it was induced with either atrial extrastimuli or burst pacing. Once AF was induced, continuous recording was performed during AF.

The atrial electrophysiological parameters were analyzed during spontaneous or induced episodes of AF lasting > 5 minutes, with the first and last minutes of AF excluded from the analysis. All right atrial catheter
recordings were scanned for periods of organized activation during AF, as defined below.

The peak-to-peak amplitude of the atrial "fibrillation waves" (F waves) was measured in lead V1, and an average amplitude was calculated over 2 seconds for every patient.

**Catheter ablation:** Only patients in whom endocardial mapping during AF showed an organized activation pattern around the tricuspid annulus were eligible for the production of cavocaval isthmus conduction block by radiofrequency ablation. Anatomically guided linear ablation of the isthmus was performed\(^{11,19-25}\) with a 6-mm-tip (Cardiac Pathways Corp, RadiT) ablation catheter. Radiofrequency pulses were delivered with the temperature preset to 60°C (Intermedics, CABL-IT) for 60 seconds. Ablation of the posterior and/or septal isthmus was performed. We confirmed the bidirectional conduction block by coronary sinus pacing and low lateral right atrial pacing. Procedural success was always confirmed under isoproterenol infusion (1 to 2 \(\mu g / \min\)). A 24-hour Holter recording was made before discharge. The ablation was considered successful if no recurrences of AF lasting > 30 seconds were present either with or without previously ineffective drugs during the follow-up.

**Follow-up:** Follow-up was conducted at the arrhythmia clinic, initially at 1 week and subsequently at 1-month intervals. A clinical examination, ECG, and Holter recordings were made every 3 months and when symptoms were suggestive of an arrhythmia recurrence. Patients with recurrent AF were managed with antiarrhythmic agents.

**Definitions:** Atrial fibrillation was defined as a rapid atrial rhythm (rate > 260 beats/minute) characterized by variability of the beat-to-beat cycle length, morphology, and/or amplitude of recorded bipolar atrial electrograms\(^{26}\). Organized activation during AF was considered present if discrete atrial complexes, separated by an isoelectric baseline, were seen during 10 or more cycles along the tricuspid annulus\(^{27}\). Despite such organization, the rhythm was still diagnostic of AF because of a variability in the beat-to-beat cycle length of > 30 msec, a variability in electrogram and surface P wave morphology, and different atrial rates in disparate portions of the atrium. In no case was atrial flutter present. Disorganized activation during AF was considered present if atrial electrograms failed to demonstrate discrete complexes or isoelectric intervals along the tricuspid annulus.

**Statistical analysis:** Results are expressed as mean \(\pm\) SD. Univariate comparisons between variables were made by Fisher's exact test for categorical variables and an unpaired \(t\) test for continuous variables. Results were con-
considered to be statistically significant when \( p < 0.05 \).

**RESULTS**

**Electrophysiological findings:** In all patients with inducible AF, 147 ± 24 seconds of AF per patient were analyzed using endocardial and 12-lead surface ECG recordings. In 16 (41%) of the 39 patients, endocardial mapping during AF showed an organized activation pattern around the tricuspid annulus more than 50% (mean, 76 ± 22%) of the time analyzed, whereas in the remaining 23 (59%) patients, this pattern was observed less than 50% (mean, 22 ± 11%) of the time. The 16 patients with an organized activation pattern around the tricuspid annulus consisted of 13 men and 3 women with a mean age of 63 ± 12 years. No structural heart disease was present in 9 patients. Hypertensive heart disease was present in 3 patients, coronary artery disease in 3 patients, and mitral valvular disease in 1 patient. Three patients had both AF and common atrial flutter, while the other 13 patients had only AF.

Among these 16 patients, in addition to sustained AF being induced, typical atrial flutter was induced in 11 patients and atypical atrial flutter was induced in 7 patients. The mean cycle length of organized AF was 198 ± 21 ms (range, 180 to 220 ms). The endocardial electrograms during AF are shown in Figure 1. Although the cycle length of atrial activity changes beat-to-beat, the activation around the tricuspid annulus shows a relatively organized atrial activity in basically the counterclockwise direction (Figure 1). Of these 16 patients, 12 showed a counterclockwise direction and 4 showed a clockwise direction. The conversion of organized AF to disorganized AF and/or disorganized AF to organized AF was observed (Figure 2).

**Ablation results:** The procedure was performed during AF in 3 patients and during sinus rhythm in 13 patients. In 2 patients, linear ablation of the cavo-tricuspid isthmus interrupted sustained AF (Figure 3). In all patients, the bidirectional conduction block was confirmed by coronary sinus pacing and low lateral right atrial pacing. After ablation, AF was no longer inducible in 13 patients. Typical atrial flutter was no longer inducible, but atypical flutter was still inducible in 3 patients.

During follow-up (mean 12 ± 3 months; range, 3 to 26 months), isthmus ablation was successful in preventing AF in 12 (75%) patients; eight without any antiarrhythmic drugs and four with a previously ineffective drug. The other four patients (25%) had AF recurrence. We did not observe the recurrence of atrial flutter during follow-up.
Figure 1. Simultaneous endocardial recordings during atrial fibrillation along the right atrial appendage (RAA), the coronary sinus (CS), and around the tricuspid annulus (TA), together with three surface ECG leads (II, III, aVF), obtained in patient 4 (left panel). Although the cycle length of atrial activity changes beat-to-beat, the activation around the tricuspid annulus shows a relatively organized atrial activity in basically a counterclockwise direction. The 45° left anterior oblique (LAO) view of the catheter positions during multisite mapping of atrial fibrillation (right panel).

Figure 2. A characteristic sequence of events in the conversion of disorganized atrial fibrillation to organized atrial fibrillation in a counterclockwise direction. Abbreviations as in Figure 1.
Comparison between success group and failure group: The parameters of the patients with successful AF ablation ($n = 12$) were compared to those in whom ablation was unsuccessful ($n = 4$). There were no significant differences between the two groups with regard to age, sex, presence of organic heart diseases, history of AF, or dimension of the left ventricle (Table I). However, the success group had a significantly higher F wave amplitude in lead V1 ($0.29 \pm 0.10$ vs $0.15 \pm 0.04$ mV, $p < 0.01$), a higher left ventricular ejection fraction ($74 \pm 9$ vs $58 \pm 2\%$, $p < 0.05$), and a smaller left atrial dimension ($35 \pm 6$ vs $43 \pm 4$ mm, $p < 0.05$) than the failure group (Table I). Figure 4 shows a representative ECG before ablation in a failure case and a successful case. In contrast to the failure case, the successful case had a higher-amplitude of F wave.

Figure 3. Example of AF interruption during radiofrequency delivery. A few seconds later, the cavo-tricuspid isthmus linear ablation interrupted sustained AF, which was not inducible after electrical stimulation and isoproterenol administration.
DISCUSSION

In 41% of patients with inducible AF, endocardial mapping during AF showed an organized activation pattern around the tricuspid annulus more than 50% of the time. The production of isthmus conduction block by radiofrequency ablation was effective in preventing paroxysmal AF in 75%

Table I. Comparison of Parameters Between 2 Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Failure (n = 4)</th>
<th>Success (n = 12)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y.o)</td>
<td>61±6</td>
<td>64±13</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>10/2</td>
<td>16/4</td>
<td>NS</td>
</tr>
<tr>
<td>OHD (+; -)</td>
<td>7:5</td>
<td>7:13</td>
<td>NS</td>
</tr>
<tr>
<td>History of AF (year)</td>
<td>3.3±2.2</td>
<td>6.2±4.9</td>
<td>NS</td>
</tr>
<tr>
<td>LVDD (mm)</td>
<td>45±2</td>
<td>47±5</td>
<td>NS</td>
</tr>
<tr>
<td>LVDS (mm)</td>
<td>31±3</td>
<td>26±6</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>58±2</td>
<td>74±9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>43±4</td>
<td>35±6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>F amplitude (mV)</td>
<td>0.15±0.04</td>
<td>0.29±0.10</td>
<td>&lt;0.01</td>
</tr>
</tbody>
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OHD = organic heart diseases; AF = atrial fibrillation; LVDD = left ventricular diastolic dimension; LVDS = left ventricular systolic dimension; LVEF = left ventricular ejection fraction; LAD = left atrial dimension.

Figure 4. Example of ECG before ablation of a failure case (panel A) and a successful case (panel B). The successful case had a higher-amplitude F wave in lead V1 (0.3 mV) than the failure case (0.1 mV).
of these patients. The success group had a significantly higher F wave amplitude in lead V1, a higher left ventricular ejection fraction, and a smaller left atrial dimension than the failure group.

**Catheter ablation of AF:** Extensive ablation, especially in the left atrium, will increase the risk of complications such as thromboembolism. Gaita, *et al.*\(^\text{10}\) performed catheter ablation only in the right atrium in patients with idiopathic AF. They created two or three linear lesions in the right atrium; 1) a septal line from the superior vena cava to the coronary ostium and from this to the inferior vena cava; 2) a cavotricuspid isthmus line; and 3) a transversal line from the fossa ovalis through the posterior wall to the lateral edge of the tricuspid annulus. However, they noticed that the third transversal line was not necessary by considering the mapping data, and did not perform the transversal lesion in the last 4 patients; ablation was successful in all cases. They were not able to confirm conduction block through the lines of lesion evaluated with atrial pacing. It is very difficult and takes a long time to make a first septal linear lesion with confirmed conduction block. In their study, it is unclear whether or not only a cavotricuspid isthmus lesion is sufficient to prevent AF. Therefore, we evaluated the ability of only an isthmus linear lesion to prevent AF, and selected patients with paroxysmal AF with organized activation around the tricuspid annulus. Our results suggest that if patients are selected by endocardial mapping data, only an isthmus lesion may be effective in such patients with paroxysmal AF.

**Rationale of isthmus ablation for AF:** The multiple reentrant wavelet hypothesis is the basis for the maze operation and catheter ablation techniques which largely mimic the maze procedure to cure chronic AF. In contrast to the multiple wavelet theory, in a mapping study in the sterile pericarditis model of paroxysmal AF, unstable reentrant circuits principally involving the septum were critical for maintenance of AF.\(^\text{18}\) In that model, ablation was made at a location so as to prevent the continued formation of mother reentrant circuits which were identified by their organized activation pattern. Thus, if the mechanism of AF is based on the unstable reentrant circuit hypothesis, linear ablation at a single site could cure this AF. The unstable reentrant circuit hypothesis, which may reflect paroxysmal AF, represents one type of mechanism associated with the maintenance of AF before it becomes chronic, i.e., before atrial remodeling transforms the mechanism to one involving multiple wavelets that may not critically involve activation around the tricuspid annulus. If AF starts due to a mechanism involving unstable reentrant circuits, ablation of the cavot-
tricuspid annulus isthmus early on before this transformation to the multiple wavelet mechanism takes place may be a useful technique to cure AF. **Predictors of successful ablation:** In the present study, the successful group had a significantly higher F wave amplitude in lead V1 than the unsuccessful group. Roithinger, *et al.* reported that a predominance of organized activation in the trabeculated right atrium influences the presence and polarity of surface F waves in lead V1.

Moreover, in our results, the successful group had a significantly higher left ventricular ejection fraction and a smaller left atrial dimension than the unsuccessful group. Left ventricular dysfunction and atrial enlargement have each been related to the spontaneous occurrence of AF in epidemiologic studies, and may represent more advanced structural disease. Some of these patients may be considered for additional ablation procedures, i.e., of the left atrium and pulmonary veins, that directly modify the substrate for AF. The absence of left ventricular dysfunction and atrial enlargement, such that there is minimal substrate for AF, possibly indicates a form of AF which is more easily cured using a single-site catheter ablation technique in the right atrium.

**Study limitations:** In the present study, endocardial mapping with limited resolution was performed. Moreover, left atrial activation was only represented by coronary sinus recordings; these activations do not necessarily reflect the left atrial endocardial activation. Recent findings have shown that the focal region in the pulmonary veins may be critically important in the genesis of AF. This could be responsible for unsuccessful ablation in the present study. However, in the successful group, focal activation originating from pulmonary veins may play a role in the onset as a trigger of AF, but may be relatively minor in the maintenance of AF. The success rates of ablation in the present study seem relatively high. Three patients had atrial flutter and AF, however, the remaining patients may have had atrial flutter that could not be detected. The prevalence of atrial flutter may be underestimated. Thus, the mechanism of AF selected in the present study was similar to that of atrial flutter.

**Conclusions:** Isthmus linear ablation may be effective in preventing paroxysmal AF with an organized activation pattern around the tricuspid annulus. Patients with paroxysmal AF having a large F wave in a surface ECG (lead V1) who do not have left ventricular dysfunction and atrial enlargement may undergo endocardial mapping around the tricuspid annulus. If these patients have an organized activation pattern around the tricuspid annulus during AF, they may be suitable for cavotricuspid isthmus ablation.
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