Randomized Study Comparing Combined Pulmonary Vein–Left Atrial Junction Disconnection and Cavotricuspid Isthmus Ablation Versus Pulmonary Vein–Left Atrial Junction Disconnection Alone in Patients Presenting With Typical Atrial Flutter and Atrial Fibrillation

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Background—Atrial flutter (AFL) and atrial fibrillation (AF) frequently coexist in the same patient. Recently it has been demonstrated that the triggers for both AF and AFL may originate in the pulmonary veins (PVs). We hypothesized that in patients with both AF and typical AFL, pulmonary vein–left atrial junction (PV-LAJ) disconnection may eliminate both arrhythmias.

Methods and Results—Consecutive patients with documented symptomatic AF and typical AFL were randomly assigned to have PV-LAJ disconnection combined with cavotricuspid isthmus (CTI) ablation (group 1, n=49) or PV-LAJ disconnection alone (group 2, n=59). Within the first 8 weeks after ablation, 32 of the group 2 patients had typical AFL documented, whereas none was seen in group 1. Twenty of these 32 converted to sinus rhythm after initiating antiarrhythmic drugs (AADs). Twelve were cardioverted, and AADs were started. After 8 weeks, all AADS were stopped, and only 3 patients continued to have recurrent sustained typical AFL that was eliminated by CTI ablation. Beyond 8 weeks of follow-up, 7 patients in group 1 and 6 patients in group 2 (14% and 11%, respectively) continued to have AF. Ten of these 13 patients underwent a repeat PV-LAJ disconnection procedure and were cured. The remaining 3 remained in normal sinus rhythm while taking AADs.

Conclusions—in patients with both AFL and AF, PV-LAJ disconnection alone may be sufficient to control both arrhythmias. CTI block reduced early postablation recurrence of arrhythmias, which in the majority of patients reflects a short-term clinical problem. (Circulation. 2003;108:2479-2483.)

Key Words: atrial flutter ▪ fibrillation ▪ catheter ablation

The success rate of maintaining sinus rhythm with pharmacological agents in patients with atrial fibrillation (AF) and atrial flutter (AFL) has been disappointing and remains a challenge.1 Recent advances in catheter-based therapy have led to a high rate of successful ablation of AFL, which is now an established therapy.2-8 The high rate of occurrence of AF after bidirectional cavotricuspid isthmus (CTI) block for treatment of typical AFL continues to be an important clinical problem and is primarily related to the presence of preexisting AF.9-11

In this subset of patients with both AF and AFL, CTI ablation and continuation of antiarrhythmic drugs (AADs) has been reported to achieve successful control of both arrhythmias and is still considered an effective and acceptable treatment approach.12-14

Recently, however, it has been demonstrated that in patients with clinical evidence of both AF and typical AFL, AF is induced by triggers from pulmonary vein (PV) foci in >85% of cases.15,16 Kumagai et al16 suggested that focal activation originating from the PVs may trigger AFL and concluded that CTI ablation combined with PV isolation should be considered in such patients.

We conducted the present study to prospectively test the hypothesis that in patients presenting with documented AF and typical AFL, pulmonary vein–left atrial junction (PV-LAJ) disconnection alone would eliminate both arrhythmias.
Methods

Study Population

Patients were consecutively identified from a population seen at 3 different institutions between January 2000 and June 2002 for the treatment of symptomatic AF/AFL. Patients with preablation evidence of both typical AFL and AF on the 12-lead surface ECG were identified. Patients had to have at least 1 documented episode of typical AFL while not taking antiarrhythmic medications. After informed consent was given, patients were assigned to have combined PV-LAJ disconnection and CTI ablation (group 1) or PV-LAJ disconnection only without CTI ablation (group 2).

Follow-Up

All patients were discharged home the next day. Warfarin was restarted in all patients the day of the procedure. All AADs were discontinued 5 half lives before ablation. Amiodarone was discontinued 4 to 5 months before the procedure in patients on this medication. Warfarin was discontinued 48 hours before the procedure, and all patients underwent transesophageal echocardiography to exclude intracardiac thrombi.

Electrophysiological Study and Ablation

All patients underwent PV-LAJ disconnection. Patients in group 1 also underwent CTI ablation after successful PV-LAJ disconnection in the same setting.

PV-LAJ Disconnection

Our approach for PV isolation has been described previously. Intracardiac echocardiographic (ICE)–guided mapping and ablation of all PV ostia was performed with the use of a 10F, 64-element, phased-array ultrasound-imaging catheter (AcuNave, Acuson) introduced through an 11F sheath through the left femoral vein. A decapolar Lasso catheter ( Biosense) was used for circular mapping and isolation of all PVs. Ablation was extended to the PV antrum in front of the tubelike portion of the pulmonary veins. Radiofrequency energy was delivered with the use of a cool-tipped ablation catheter (EP Technologies). Energy delivery was titrated, with the operator watching for microbubble formation. Two types of bubble patterns were seen with ICE: (1) scattered microbubbles, reflecting early tissue overheating (type 1), and (2) brisk shower of dense microbubbles (type 2), reflecting impending impedance rise. When the type 1 microbubble pattern was seen, energy was titrated down by 5-W decrements until microbubble generation subsided. Energy delivery was stopped when type 2 microbubbles were seen.

Intravenous heparin was administered during the procedure in all patients.

CTI Block

Radiofrequency ablation was performed under anatomic and electrogram guidance. The protocol used to assess bidirectional conduction block across the cavitricuspid line has been described before. Briefly, we proved the existence of double potentials along the ablation line separated by ≥100 ms during sinus rhythm. We also assessed bidirectional block by pacing from both sides of the ablation line (coronary sinus ostium and lateral isthmus [7 o’clock position in 60° left anterior oblique]).

Follow-Up

Warfarin was restarted in all patients the day of the procedure. All patients were discharged home the next day.

Follow-up was scheduled at 1, 3, 6, and 12 months. A loop recorder was used in all patients to monitor events during the first month after ablation and was repeated 3 months after ablation. Patients were also monitored with Holter recordings before discharge and at 3, 6, and 12 months of follow-up. Additional event recorder monitoring was considered beyond the 3-month period for patients and at 3, 6, and 12 months of follow-up. Additional event recorder was used in all patients to monitor events during the first month after ablation and was repeated 3 months after ablation.

Results

Study Population

Of 660 patients seen for symptomatic AF between January 2000 and June 2002, 108 patients (16%) with documentation of both typical AFL and AF were identified. Of these 108 patients, 49 had CTI ablation in addition to PV-LAJ disconnection (group 1). Group 2 comprised the other 59 patients, who had PV-LAJ disconnection alone.

Statistical Analysis

Continuous variables are expressed as mean±SD. Continuous variables were compared by Student’s t test. Differences among groups of continuous variables were determined by ANOVA. Categorical variables were compared by χ2 analysis or with Fisher’s exact test. A Kaplan-Meier analysis was used to determine the probability of freedom from recurrent AF and AFL. The Kaplan-Meier curves presented ignore the blanking period of 8 weeks after ablation. Results with values of P<0.05 were considered statistically significant.

Results

Study Population

Of 660 patients seen for symptomatic AF between January 2000 and June 2002, 108 patients (16%) with documentation of both typical AFL and AF were identified. Of these 108 patients, 49 had CTI ablation in addition to PV-LAJ disconnection (group 1). Group 2 comprised the other 59 patients, who had PV-LAJ disconnection alone.
The characteristics of the study population are described in Table 1. All the patients had failed AADs or had intolerable side effects. The mean duration of symptoms was 6±4 years and 5±3 years in groups 1 and 2, respectively.

The left ventricular ejection fraction in both groups was comparable, 52±4% and 53±4% in groups 2 and 1, respectively.

In group 1, 30 patients had paroxysmal AF, 6 had persistent AF, and 13 had permanent AF. This was not significantly different from group 2, who had 34, 5, and 20 patients with paroxysmal, persistent, and permanent AF, respectively.

**Follow-Up**

Table 2 lists the follow-up results of all study patients. No episode of typical AFL was seen in group 1 patients. Early recurrence of AF episodes, defined as recurrence of AF within 8 weeks after PV-LAJ disconnection, was observed in 35% (16 of 49 patients) of group 1. In all these patients with early recurrence, pharmacological and/or DC cardioversion was attempted, and AADs were given for 8 weeks. Fourteen percent (7 of 49) of patients in group 1 continued to have AF after stopping the AADs. Five of these 7 patients were found to have recovered PV potentials during a second electrophysiological study. These patients were successfully treated with repeat PV-LAJ disconnection. The remaining 2 patients were maintained in normal sinus rhythm while receiving previously ineffective AADs.

In 55% (32 of 59) of patients in group 2, episodes of typical AFL was documented within 8 weeks after PV-LAJ disconnection (mean, 2±3 weeks). Eighteen of these patients also had episodes of AF documented in this period of early follow-up. Twenty (9 with AF/AFL and 11 with AFL only) of these 32 patients converted spontaneously to sinus rhythm after initiating a class I drug (8 patients), sotalol (11 patients), or dofetilide (1 patient) for 8 weeks. In the remaining 12 patients (9 with AF/AFL and 3 with AFL only), DC cardioversion was performed and patients were started on a class I drug (5 patients) or sotalol (7 patients). All AADs were discontinued 8 weeks after PV-LAJ disconnection. Only 5% (3 of 59) of patients in group 2 continued to have recurrent sustained AFL without any clinical evidence of AF. In these 3 patients, a CTI line was performed to eliminate this arrhythmia. Eleven percent (6 of 59) of patients in group 2 continued to have AF after stopping the AADs. Five of these 6 patients were found to have recovered PV potentials during a second electrophysiological study. These patients were successfully treated with repeat PV-LAJ disconnection. The remaining 1 patient was maintained in normal sinus rhythm while receiving previously ineffective AADs.

None of the patients had thromboembolic complications. There was no occurrence of severe PV stenosis (>70%). One patient in each group had moderate (50% to 70%) asymptomatic PV stenosis.
Comparative Recurrence of Arrhythmia

Figures 1 and 2 depict recurrences of arrhythmia on follow-up.

Recurrence of AFL

In 55% (32 of 59) of group 2 patients, episodes of typical AFL were documented within 8 weeks after PV-LAJ disconnection (mean, 2 ± 3 weeks). No episode of typical AFL recurrence was seen in group 1 patients. Beyond 8 weeks, only 5% (3 of 59) of patients in group 2 continued to have recurrent sustained AFL without any clinical evidence of AF.

During the first 8 weeks, atypical AFL was seen in only 1 group 1 patient. This was terminated with cardioversion and did not recur.

Recurrence of AF

Early recurrence of AF episodes, defined as recurrence of AF within 8 weeks after PV-LAJ disconnection, was observed in 35% (16 of 49 patients) of group 1 and 30% (18 of 59 patients) of group 2 patients (P = NS). As described above in all patients with early recurrence, pharmacological and/or DC cardioversion was attempted and AADs were given for 8 weeks. Fourteen percent (7 of 49) of patients in group 1 and 11% (6 of 59) of patients in group 2 continued to have AF after stopping the AADs (P = NS).

Discussion

To our knowledge, this is the first study to assess the outcome of PV-LAJ disconnection in patients presenting with both typical AFL and AF. In our study, the long-term AF/AFL cumulative free rate was independent of bidirectional isthmus block in patients presenting with documentation of both typical AFL and AF on 12-lead surface ECG. It is known from clinical experience that treatment of AF with antiarrhythmic medications can result in AFL.12–14 This has been postulated to be secondary to the development of functional block forcing the wave front of activation to follow a pathway, hence producing a stable rhythm such as AFL. Ortiz et al,19 in a canine model, demonstrated that the spontaneous transformation of AF to AFL was related to the development of a line of functional block. This phenomenon could be enhanced by the use of AADs, as has been proven in both experimental and human studies. In addition, AFL and AF often coexist. The above two phenomena (that is, the conversion of AF into AFL by AADs and the coexistence of these two arrhythmias together with periodic transition from one to the other in the same patient) have led investigators to postulate that hybrid therapy with AADs and CTI ablation may control both arrhythmias.12–14,20

However, the rate of AF recurrence after isthmus ablation alone has been as high as 80% and up to 30% in those continued on medical therapy after isthmus ablation.9–12,20 Because of the high rates of recurrence of AF, more definitive interventions were pursued. Recently, Hsieh et al15 demonstrated that isthmus ablation in addition to PV isolation was safe and effective, with no recurrence of AF or AFL at follow-up. Similarly, Kumagai et al16 showed that combined
ablation eliminated AF in 69% of patients, with no need for medical therapy. However, the need for isthmus ablation at the time PV isolation for AF was not assessed. In our study, early recurrence of AFL alone occurred in 24% (14 of 59) of patients who underwent PV isolation only. Although these patients required further therapy during the first 8 weeks, their subsequent clinical course remained favorable.

Our study suggests that PV triggers appear to initiate AFL. Careful human and animal studies have demonstrated that AF usually precedes the onset of AFL.21–24 Roithinger et al24 postulated that the mechanism of AFL in patients presenting with both AFL and AF could be organization of AF to AFL as a result of coalescence of fibrillatory wavelets around anatomic barriers along the crista terminalis and Eustachian valve. Recent studies have demonstrated the crucial role of pulmonary vein triggers for the initiation of AF.7,25,26 These studies, together with our findings and those of others,15,16 allow us to speculate on the following mechanism: PV triggers initiate disorganized AF. This then becomes organized and subsequently, because of anatomic and electrical barriers, the right atrium is activated by a single wavelet, giving rise to AFL, as proposed by Roithinger et al.24 Indeed, PV triggers may be responsible for the development of AFL, given the right conditions.

Limitations
Isolation of all 4 pulmonary veins is technically challenging. However, these procedures were performed at highly specialized centers with experienced operators and uniform ablation approach. The results of this study may not be reproducible in the community because of this issue. This study does not include follow-up beyond 1 year.

Conclusions
Our results suggest that in most patients with both AF and typical AFL, cure of AF will eliminate AFL as well. These findings provide new insight into the understanding of these arrhythmias and indicate that AF and typical AFL usually share common triggers.

CTI block reduced early recurrence of AFL, which in the majority of patients did not represent a long-term problem and required only short-term therapy.

References
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Circulation. 2003;108:2479-2483; originally published online November 10, 2003; doi: 10.1161/01.CIR.0000101684.88679.AB

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

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