Atrial Fibrillation After Radiofrequency Ablation of Type I Atrial Flutter
Time to Onset, Determinants, and Clinical Course
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Background—The occurrence of atrial fibrillation after ablation of type I atrial flutter remains an important clinical problem. To gain further insight into the pathogenesis and significance of postablation atrial fibrillation, we examined the time to onset, determinants, and clinical course of atrial fibrillation after ablation of type I flutter in a large patient cohort.

Methods and Results—Of 110 consecutive patients with ablation of type I atrial flutter, atrial fibrillation was documented in 28 (25%) during a mean follow-up of 20.1±9.2 months (cumulative probability of 12% at 1 month, 23% at 1 year, and 30% at 2 years). Among 17 clinical and procedural variables, only a history of spontaneous atrial fibrillation (relative risk 3.9, 95% confidence intervals 1.8 to 8.8, P=0.001) and left ventricular ejection fraction ≤50% (relative risk 3.8, 95% confidence intervals 1.7 to 8.5, P=0.001) were significant and independent predictors of subsequent atrial fibrillation. The presence of both these characteristics identified a high-risk group with a 74% occurrence of atrial fibrillation. Patients with only 1 of these characteristics were at intermediate risk (20%), and those with neither characteristic were at lowest risk (10%). The determinants and clinical course of atrial fibrillation did not differ between an early (≤1 month) compared with a later onset. Atrial fibrillation was persistent and recurrent, requiring long-term therapy in 18 patients, including 12 of 19 (63%) with prior atrial fibrillation and left ventricular dysfunction.

Conclusions—Atrial fibrillation after type I flutter ablation is primarily determined by the presence of a preexisting structural and electrophysiological substrate. These data should be considered in planning postablation management. The persistent risk of atrial fibrillation in this population also suggests a potentially important role for atrial fibrillation as a trigger rather than a consequence of type I atrial flutter. (Circulation. 1998;98:315-322.)

Key Words: atrial fibrillation □ atrial flutter □ catheter ablation

Catheter ablation of type I atrial flutter directed at a protected isthmus of atrial tissue between the tricuspid valve annulus and the eustachian ridge, which constitutes an obligate portion of the flutter circuit, has emerged as an effective therapeutic option.1-12 During the evolution of this procedure, diverse approaches have been taken to the identification, location, and extent of target sites within the annular–eustachian ridge isthmus. Initial experience with the end points of flutter termination during radiofrequency energy application and subsequent noninduction of type I atrial flutter were associated with a variable risk of recurrence (10% to 30%).1-6 More recent reports indicate that the production and demonstration of bidirectional conduction block through the annular–eustachian ridge isthmus may lower this risk considerably.7,8,10-12

Despite technical refinements and improved long-term efficacy of the ablation procedure, the subsequent occurrence of atrial fibrillation remains a significant clinical problem. It is reported to follow 18% to 30% of ablation procedures,4,5,8,10,13,14 often within the first month, and may be an important cause of recurrent symptoms and renewed or continued antiarrhythmic therapy. However, detailed information regarding the frequency, duration, and therapy of atrial fibrillation in individual patients is limited. A contributing role by the procedure remains a concern, although preliminary data indicate that atrial fibrillation is more common in patients with a history of this arrhythmia.5,8,13,14

Improved identification of patients at high risk for subsequent atrial fibrillation may facilitate optimal patient selection for flutter ablation and permit more effective use of additional or adjunctive therapies after ablation. In addition, this population provides the opportunity to examine the pathophysiologic links between these 2 arrhythmias. The purpose of this study was to characterize the onset, determinants, and clinical course of postablation atrial fibrillation. In addition, we examined potential differences in the clinical significance and determinants of atrial fibrillation as a function of time after the procedure.

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Methods

Study Population
The study population consisted of 110 consecutive patients who underwent radiofrequency catheter ablation for recurrent type I atrial flutter from July 1994 to June 1997. Each patient had recurrent flutter or unacceptable side effects during 1 to 3 previous antiarrhythmic drug trials. Previous episodes of atrial fibrillation were not considered a contraindication to atrial flutter ablation if it they were infrequent and not the predominant clinical arrhythmia (see “Results”). Vigorous attempts were made to obtain documentation of all prior atrial arrhythmias.

Two-dimensional and M-mode echocardiographic assessment was obtained within 1 month of the ablation procedure in all patients. Echocardiograms were analyzed by independent observers without knowledge of the clinical outcome. Left ventricular hypertrophy was defined as left ventricular wall thickness exceeding that predicted for body surface area. Left ventricular dysfunction was considered present if the left ventricular ejection fraction was <50%. Left atrial enlargement was considered present if the dimensions exceeded that predicted for body surface area (2.4 cm/m²). Right atrial enlargement was assessed qualitatively.

Electrophysiological Study
Written informed consent was obtained before electrophysiological study and radiofrequency catheter ablation in all patients. Electrophysiological study was performed after discontinuation of all antiarrhythmic drugs for at least 5 half-lives except in patients treated with amiodarone at the time of the procedure. Five multipolar catheters were inserted from the right and left femoral veins and the right internal jugular vein. One quadrupolar catheter was positioned in the right atrial appendage (and repositioned to the right ventricular outflow tract during ablation). An octopolar catheter (Cordis-Webster) was positioned at the His bundle and a decapolar catheter (Bard-USCI, 2–5-mm intervals) was positioned in the coronary sinus, with the proximal electrode pair located at the ostium. A deflectable quadripolar catheter (Cordis Webster, 2–5-mm spacing) was positioned at the inferolateral tricuspid annulus for pacing and recording from the lateral isthmus. Annullar activation during atrial flutter or atrial pacing was assessed by either a second roving deflectable quadripolar catheter, or a 20-electrode Halo catheter (Cordis Webster, 2–7-mm intervals). Patients were studied in the fasting state and sedated with intravenous midazolam and fentanyl. An initial bolus of heparin (2000 U) was administered after the insertion of catheters, followed by 1000 U/h until completion of the study. Noninvasive blood pressure and oxygen saturation were monitored continuously.

Simultaneous surface 12-lead ECGs and bipolar intracardiac ECGs were continuously acquired with a filter bandwidth of 30 to 500 Hz, digitized (1000 samples/s), and displayed on a high-resolution video monitor at 200 mm/s for inspection and subsequent review (Prucka Engineering). Data were stored on optical disk for retrieval and off-line analysis.

For patients in atrial flutter at the onset of the procedure, mapping and pacing during atrial flutter was performed before pace termination and reinduction. Burst pacing was performed in sinus rhythm at 2 atrial sites (proximal coronary sinus and inferolateral tricuspid annulus). Burst pacing was performed at cycle lengths of 600, 500, and 400 ms, then progressively shortened by 10 ms/burst until 2:1 atrial capture or the induction of atrial flutter or atrial fibrillation. If type I atrial flutter was not induced, programmed atrial stimulation with up to 2 extrastimuli was also performed, including additional right atrial sites. During spontaneous or induced flutter, pacing was performed at multiple sites within the annular–eustachian ridge isthmus to verify participation of the isthmus in the flutter circuit.

Type I atrial flutter was induced in 108 of 110 patients, counterclockwise only in 52, clockwise only in 6, and both in 50. The mean cycle length of counterclockwise flutter was 245 ± 32 ms, and the mean cycle length of clockwise flutter was 242 ± 35. Atrial fibrillation lasting >30 seconds was induced in 31 patients. Atypical atrial flutter (see “Definitions”) lasting >30 seconds was induced in 24 patients.

Ablation
The method of ablation was anatomic, with the primary goal to produce a line of conduction block between the tricuspid annulus and the eustachian ridge/inferior vena cava. The ablation catheters had distal electrodes of 4 mm (19 patients), 5 mm (3 patients), or 8 mm (88 patients). The output of a radiofrequency generator (Radionics) was delivered to the distal pole of the ablation catheter and 1 or 2 posteriorly positioned adhesive electrosurgical dispersive pads. Radiofrequency energy was applied with an initial power of 30 W and was progressively increased to a maximum of 45 W (4 to 5 mm tip) or 60 W (8 mm tip) during continuous impedance monitoring. Energy application was continued for 30 to 60 ms or until an impedance rise was observed. A line of sequential overlapping lesions was given beginning at the tricuspid valve annulus, with stepwise withdrawal of the catheter until the last lesion was delivered at the eustachian ridge/inferior vena cava. Radiofrequency energy was applied during flutter in 108 patients and during sinus rhythm in the 2 patients without inducible or spontaneous flutter at the time of the procedure. In the initial 16 patients, only termination of flutter during radiofrequency application and subsequent noninduction of type I flutter was used as the procedural end point. In the subsequent 94 patients, including the 2 patients without inducible or spontaneous flutter at the time of the procedure, an additional goal of ablation was to produce bidirectional conduction block through the annular–eustachian ridge isthmus (see below).

Follow-up
After catheter ablation, all patients underwent continuous ECG monitoring for at least 24 hours before hospital discharge. Class I or III antiarrhythmic drugs were not prescribed in 104 patients. In 6 patients, amiodarone had been initiated before the procedure for control of atrial fibrillation and was continued. Outpatient follow-up and electrocardiograms were performed at 1 month and at 4- to 6-month intervals thereafter. Patients were encouraged to contact 1 of the investigators at any time for recurrent symptoms or palpitations. Patients with palpitations underwent additional Holter or transtelephonic ambulatory ECG monitoring. Records from hospital and clinic visits at other institutions were periodically reviewed for evidence of recurrent atrial arrhythmias. Transtelephonic monitoring in asymptomatic patients was not routinely performed. Patients received aspirin 325 mg daily unless there existed an indication for systemic anticoagulation with warfarin.

Definitions
Counterclockwise type I atrial flutter was considered present if counterclockwise activation around the tricuspid annulus was demonstrated (as viewed in the left anterior oblique projection) and concealed entrainment could be demonstrated from annular pacing sites within the tricuspid valve-eustachian ridge isthmus, with a postspacing interval similar to the flutter cycle length. The surface ECG generally demonstrated negative flutter waves in leads II, III, and aVF, and isoelectric or positive flutter waves in lead V1. Clockwise type I atrial flutter was considered present if clockwise activation around the tricuspid annulus was demonstrated and concealed entrainment could be demonstrated from annular pacing sites within the tricuspid valve–eustachian ridge isthmus, with a postspacing interval similar to the flutter cycle length. Flutter waves were generally positive or biphasic in leads II, III, and aVF, with varying morphology in V1. Atypical atrial flutter was defined as all other flutters with a stable activation sequence and atrial intervals in which participation of the isthmus in the circuit was excluded by the above criteria.

Bidirectional isthmus conduction block was considered present when the following conditions were met: (1) pacing during sinus rhythm from inferolateral tricuspid annulus posterior and lateral to the ablation line resulted in sequential clockwise activation of the tricuspid annulus, with late activation of the atrium in the His
bundle recording and latest activation in the proximal coronary sinus, and (2) pacing in sinus rhythm from the proximal coronary sinus resulted in sequential counterclockwise activation of the tricuspid annulus, with early activation of the atrium in the His bundle recording and latest activation at the inferolateral tricuspid annulus site. In all instances, activation around the annulus was assessed by recordings from multiple sites.

**Statistical Analysis**

Descriptive data are presented as mean±SD or as frequencies. Univariate comparisons between variables were made by Fisher’s exact test for categorical variables and unpaired t test for continuous variables. The actuarial probability of freedom from atrial fibrillation after ablation was calculated with the method of Kaplan and Meier. Baseline clinical and procedural variables were subsequently subjected to multivariate analysis with a Cox proportional hazards model and stepwise backward selection to identify significant and independent predictors of time to onset of postablation atrial fibrillation. Variables in the initial model included age, sex, symptom duration, functional class, history of atrial fibrillation, preablation treatment with class I or III antiarrhythmic drugs, presence of structural heart disease, left ventricular ejection fraction, presence of left ventricular dysfunction, left ventricular hypertrophy, atrial enlargement, presence of bidirectional isthmus conduction block at the end of the procedure, number of radiofrequency energy applications, catheter tip size, induced atrial fibrillation and induced atypical flutter during electrophysiological study, and antiarrhythmic drug treatment at discharge. Survival analysis and Cox regression were performed with Systat 7.0 statistical software (SPSS Inc). A value of P<0.05 was considered significant.

**Results**

**Study Population**

Baseline patient characteristics are summarized in Table 1. There were 86 men and 24 women with a mean age of 62±14 years. Structural heart disease was present in 71 patients (65%). Coronary artery disease was present in 33 patients (including 15 with remote surgical revascularization), nonischemic cardiomyopathy in 16 patients, valvular heart disease in 13 patients, congenital heart disease in 5 patients, right ventricular cardiomyopathy in 2 patients, and hypertrophic cardiomyopathy in 2 patients. The mean left ventricular ejection fraction was 50±14%, and left ventricular dysfunction was present in 44 patients (40%). Atrial enlargement was present in 54 patients (49%): left atrial only in 26, right atrial only in 13, and bialtal in 15. The mean duration of symptoms before flutter ablation was 2.2±36 months (range 1 to 161 months). Forty-five patients (41%) had received at least 1 class I or III antiarrhythmic drug before the ablation procedure, including amiodarone in 15 patients. The remaining patients received 1 or more trials of β-blockers, Ca2+ channel blockers, and/or digoxin.

Spontaneous atrial fibrillation was documented in 44 patients (40%) before the ablation procedure. In 23 patients only a single episode was documented. In 15 patients, more than 1 prior episode of atrial fibrillation was documented; in each of these patients, episodes of documented flutter exceeded fibrillation by a ratio of at least 3:1. In 6 patients (5%), recurrent atrial fibrillation was the initial presenting arrhythmia that was subsequently suppressed by amiodarone. In each of these 6 patients, only atrial flutter was observed in the 3 months preceding the ablation procedure. Overall, 20 of 44 patients (45%) with a history of atrial fibrillation had received prior treatment with class I or III antiarrhythmic drug therapy.

**Atrial Flutter Recurrence**

All patients were followed for a minimum of 4 months, with a mean follow-up duration of 20.1±9.2 months. One of the 2 patients with persistently inducible flutter continued to have frequent spontaneous episodes and underwent AV nodal ablation and implantation of a permanent pacemaker. Type I atrial flutter recurred in 9 of 108 patients with successful ablation and implantation of a permanent pacemaker. Each had bidirectional conduction block at the end of the procedure. Four patients with recurrent type I flutter underwent a second procedure. Each had bidirectional conduction through the isthmus. Two patients in whom prior success was judged by noninduction alone had relatively large areas (>1 cm) of sharply defined single electrograms during atrial flutter adjacent to the prior site of ablation. Two patients in whom prior success was judged by the presence of bidirectional isthmus conduction block had either no potentials or double potentials recorded during flutter along most of the previous ablation line. However, each had a relatively discrete area of single electrograms located in the mid or posterior isthmus. Additional radiofrequency energy applications produced bidirectional conduction block in all 4 patients, and none have had

**TABLE 1. Patient Characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD or Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62 ± 14</td>
</tr>
<tr>
<td>Sex, n male</td>
<td>86 (78%)</td>
</tr>
<tr>
<td>Symptom duration, mo</td>
<td>25 ± 36</td>
</tr>
<tr>
<td>Prior class I or III AAD, n</td>
<td>45 (41%)</td>
</tr>
<tr>
<td>Functional class I–III, n</td>
<td>31 (28%)</td>
</tr>
<tr>
<td>Preablation ATR FIB, n</td>
<td>44 (40%)</td>
</tr>
<tr>
<td>Structural HD, n</td>
<td>71 (65%)</td>
</tr>
<tr>
<td>LVEF, %±SD</td>
<td>50 ± 14</td>
</tr>
<tr>
<td>LVEF &lt;50%, n</td>
<td>44 (40%)</td>
</tr>
<tr>
<td>Left ventricular hypertrophy,n</td>
<td>38 (35%)</td>
</tr>
<tr>
<td>Atrial enlargement, n</td>
<td>54 (49%)</td>
</tr>
</tbody>
</table>

AAD indicates antiarrhythmic drugs; ATR FIB, atrial fibrillation; HD, heart disease; and LVEF, left ventricular ejection fraction.
further recurrences during follow-up. One patient who declined a second procedure had infrequent recurrences on a class I antiarrhythmic drug. Only 1 patient with recurrent type I flutter also had atrial fibrillation documented during follow-up.

Three patients had spontaneous atypical atrial flutter during follow-up. Each of these patients also had postablation atrial fibrillation. The diagnosis of atypical flutter was confirmed by follow-up electrophysiological study in all 3 patients, and each had persistent bidirectional isthmus conduction block. Only 1 of these patients had atypical flutter documented during the initial electrophysiological study.

**Postablation Atrial Fibrillation**

Spontaneous atrial fibrillation occurred in 28 of 110 patients (25%) during follow-up. In 13 of these patients (46%), atrial fibrillation occurred within the first month after ablation (early atrial fibrillation), and the remainder occurred from 2 to 22 months after the procedure (late atrial fibrillation). The cumulative probability of postablation atrial fibrillation was 12% at 1 month, 23% at 1 year, and 30% at 2 years (Figure 1). By univariate analysis, several preablation clinical variables known to be associated with atrial fibrillation in other populations significantly influenced the probability of atrial fibrillation during follow-up. Patients with postablation atrial fibrillation were significantly older and had a greater frequency of preablation atrial fibrillation, left ventricular dysfunction, and atrial enlargement (Table 2). The risk of atrial fibrillation was similar whether atrial enlargement was left atrial alone, right atrial alone, or biatrial. For the purpose of subsequent analysis, atrial enlargement was considered as a single variable. Of procedural variables, only the induction of atrial fibrillation during electrophysiological testing significantly influenced the likelihood of subsequent spontaneous atrial fibrillation.

Predictors of postablation atrial fibrillation were further evaluated by multivariate Cox regression. Two variables were significantly and independently associated with the onset of postablation atrial fibrillation, a history of spontaneous atrial fibrillation (relative risk 3.9, 95% confidence intervals 1.8 to 8.8, \( P=0.001 \)), and left ventricular ejection fraction <50% (relative risk 3.8, 95% confidence intervals 1.7 to 8.5, \( P=0.001 \)). The additive risk associated with these 2 variables is illustrated in Figure 2. In patients with normal ventricular function and no history of atrial fibrillation, postablation atrial fibrillation was uncommon (4 of 41 patients [10%]). Patients with only 1 of the 2 variables (left ventricular ejection fraction <50% or a history of spontaneous atrial fibrillation) had a significantly higher risk of atrial fibrillation (Table 2).

**TABLE 2. Univariate Predictors of Postablation Atrial Fibrillation**

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>Atrial Fibrillation (n=28)</th>
<th>No Atrial Fibrillation (n=82)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y ± SD</td>
<td>66 ± 10</td>
<td>61 ± 15</td>
<td>0.046</td>
</tr>
<tr>
<td>Sex, n male</td>
<td>23 (82%)</td>
<td>63 (77%)</td>
<td>NS</td>
</tr>
<tr>
<td>Symptom duration, mo ± SD</td>
<td>33 ± 36</td>
<td>23 ± 35</td>
<td>NS</td>
</tr>
<tr>
<td>Prior class I or III AAD, n</td>
<td>13 (46%)</td>
<td>32 (39%)</td>
<td>NS</td>
</tr>
<tr>
<td>Functional class II–III, n</td>
<td>9 (32%)</td>
<td>22 (27%)</td>
<td>NS</td>
</tr>
<tr>
<td>Preablation ATR FIB, n</td>
<td>20 (71%)</td>
<td>24 (29%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Structural HD, n</td>
<td>20 (71%)</td>
<td>51 (62%)</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF, % ± SD</td>
<td>45 ± 13</td>
<td>52 ± 14</td>
<td>0.025</td>
</tr>
<tr>
<td>LVEF &lt;50%, n</td>
<td>19 (68%)</td>
<td>25 (30%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Left ventricular hypertrophy, n</td>
<td>12 (43%)</td>
<td>26 (32%)</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial enlargement, n</td>
<td>21 (75%)</td>
<td>33 (40%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Procedural variables

- Isthmus block,* n | 23 (82%) | 67 (82%) | NS |
- RF applications, n ± SD | 16 ± 6 | 13 ± 7 | NS |
- 8-mm-tip catheter, n | 22 (79%) | 66 (80%) | NS |
- Induced ATR FIB, n | 13 (46%) | 18 (22%) | 0.021|
- Induced ATYP FLU,† n | 7 (25%) | 17 (21%) | NS |

Follow-up variables

- Discharge AAD, n | 3 (11%) | 3 (4%) | NS |
- Follow-up duration, mo ± SD | 17.8 ± 10 | 18.3 ± 9 | NS |

*Bidirectional isthmus conduction block demonstrated at the end of ablation (see “Definitions”).
†Non–isthmus-dependent flutter (see “Definitions”).

\( P=0.001 \). The additive risk associated with these 2 variables is illustrated in Figure 2. In patients with normal ventricular function and no history of atrial fibrillation, postablation atrial fibrillation was uncommon (4 of 41 patients [10%]). Patients with only 1 of the 2 variables (left ventricular ejection fraction <50% or a history of spontaneous atrial fibrillation) had a significantly higher risk of atrial fibrillation (Table 2).

[Figure 1. Kaplan-Meier cumulative probability of survival free of atrial fibrillation during follow-up. Numbers in italics indicate the number of patients at risk at various points during follow-up.]

[Figure 2. Risk of atrial fibrillation during follow-up as a function of a prior history of atrial fibrillation and left ventricular dysfunction. Bars indicate the proportion of each of 4 patient subgroups that developed atrial fibrillation. Numerical proportions are in italics within each bar. AF indicates atrial fibrillation; LVEF, left ventricular ejection fraction.]
dysfunction alone or previous atrial fibrillation alone) were at intermediate risk of postablation atrial fibrillation (20%). Patients with both findings had a high likelihood of developing postablation atrial fibrillation (14 of 19 patients [74%]).

**Early Versus Late Atrial Fibrillation**

We also evaluated potential differences in the determinants and clinical course of atrial fibrillation occurring early (within 1 month of ablation) compared with onset later during follow-up. None of the clinical, procedural, or follow-up characteristics differed between the 2 groups of patients (Table 3). Patients with early atrial fibrillation had a slight excess of structural heart disease, preablation atrial fibrillation, and left ventricular hypertrophy. These trends were not statistically significant.

There was no difference in the clinical course of patients with early compared with a late onset of postablation atrial fibrillation. Of the 13 patients with early-onset atrial fibrillation, 8 had episodes that were persistent and recurrent beyond the initial month, requiring 1 or more cardioversions. Of these 8 patients, 6 were ultimately placed on amiodarone treatment and have subsequently remained in sinus rhythm, and 2 underwent AV nodal ablation and permanent pacing. One patient had a single episode of persistent atrial fibrillation and was placed on a class I antiarrhythmic after cardioversion. The drug was stopped after 1 month, and no further symptomatic episodes have occurred. Four patients had infrequent self-terminating episodes of atrial fibrillation (<24-hour duration) and were never cardioverted or placed on antiarrhythmic drugs therapy. In 2 of these 4 patients, occasional brief episodes persisted beyond 3 months.

The clinical course of the 15 patients with late-onset atrial fibrillation was similar. Ten patients had episodes that were persistent and recurrent beyond 1 month of initial onset, requiring 1 or more cardioversions. Of these 10 patients, sinus rhythm was ultimately maintained with amiodarone in 7, sotalol in 1, a class I antiarrhythmic in 1, and 1 patient underwent AV node ablation and placement of a permanent pacemaker. Two patients were cardioverted for a single episode of persistent atrial fibrillation, and after brief antiarrhythmic therapy, remained in sinus rhythm without antiarrhythmic drugs. The 3 other patients had only infrequent self-terminating episodes of atrial fibrillation (<24-hour duration), and did not receive antiarrhythmic drug therapy. In 1 of the 3 patients, occasional brief episodes persisted more than 3 months after the initial onset.

Overall, at the end of follow-up, 18 patients required long-term therapy for control of symptomatic postablation atrial fibrillation: antiarrhythmic therapy in 15 patients and ablation and pacing in 3 patients. Twelve of 19 patients (63%) with left ventricular dysfunction and a history of atrial fibrillation required long-term therapy for postablation atrial fibrillation. In contrast, only 6 of 91 (7%) with only 1 or neither of these preprocedure risk factors required additional long-term therapy ($P<0.001$).

**Discussion**

**Major Findings**

This study confirms previous observations of a moderately high incidence of symptomatic postablation atrial fibrillation (30% probability at 2 years) despite a low recurrence of type I atrial flutter (5% overall, 2.2% in patients with bidirectional isthmus conduction block). Although episodes of atrial fibrillation were often transient, in two thirds of patients the episodes were persistent and recurrent, ultimately requiring long-term therapy. Risk could be stratified by the presence or absence of 2 independent and significant predictors, prior atrial fibrillation (3.9-fold increased risk), and left ventricular dysfunction (3.8-fold increased risk). The presence of both these clinical characteristics identified a high-risk group of which 74% developed atrial fibrillation during follow-up. Patients with only 1 of these characteristics were at intermediate risk (20%), and those without prior atrial fibrillation and with normal ventricular function were at lowest risk (10%) for subsequent atrial fibrillation. Further, patients in the high-risk group accounted for the majority of patients requiring long-term therapy for control of recurrent fibrillation. Although the initial onset of atrial fibrillation was greatest in the first month after ablation, neither the clinical course nor risk factors differed by time of onset.

**Determinants of Atrial Fibrillation**

Age,20,21 left ventricular dysfunction,21–23 and atrial enlargement21–23 have each been related to the spontaneous occurrence of atrial fibrillation in epidemiologic studies; thus their significance as univariate predictors of postablation atrial fibrillation in this study is not surprising. Structural heart

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**Table 3. Comparison of Early vs Late Atrial Fibrillation**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early Atrial Fibrillation (n=13)</th>
<th>Late Atrial Fibrillation (n=15)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y, SD</td>
<td>66±11</td>
<td>64±10</td>
<td>NS</td>
</tr>
<tr>
<td>Sex, n male</td>
<td>10 (83%)</td>
<td>13 (87%)</td>
<td>NS</td>
</tr>
<tr>
<td>Symptom duration, mo±SD</td>
<td>39±42</td>
<td>28±35</td>
<td>NS</td>
</tr>
<tr>
<td>Functional class II–III, n</td>
<td>5 (38%)</td>
<td>4 (27%)</td>
<td>NS</td>
</tr>
<tr>
<td>Prior class I or III AAD, n</td>
<td>5 (38%)</td>
<td>8 (53%)</td>
<td>NS</td>
</tr>
<tr>
<td>Preablation ATR FIB, n</td>
<td>10 (77%)</td>
<td>10 (67%)</td>
<td>NS</td>
</tr>
<tr>
<td>Structural HD, n</td>
<td>10 (77%)</td>
<td>10 (67%)</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial enlargement, n</td>
<td>10 (77%)</td>
<td>11 (73%)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Procedural variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isthmus block,* n</td>
<td>11 (85%)</td>
<td>12 (80%)</td>
<td>NS</td>
</tr>
<tr>
<td>RF applications, n±SD</td>
<td>17±7</td>
<td>14±6</td>
<td>NS</td>
</tr>
<tr>
<td>8-mm-tip catheter, n</td>
<td>10 (77%)</td>
<td>12 (80%)</td>
<td>NS</td>
</tr>
<tr>
<td>Induced ATR FIB, n</td>
<td>6 (46%)</td>
<td>7 (47%)</td>
<td>NS</td>
</tr>
<tr>
<td>Induced ATYP FLU,† n</td>
<td>4 (31%)</td>
<td>3 (20%)</td>
<td>NS</td>
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<tr>
<td><strong>Follow-up variables</strong></td>
<td></td>
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<tr>
<td>Discharge AAD, n</td>
<td>2 (15%)</td>
<td>1 (7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up after first ATR</td>
<td>15.9±6.2</td>
<td>13.0±7.1</td>
<td>NS</td>
</tr>
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</table>

*Abbreviations and footnotes as in Tables 1 and 2.*
Atrial Fibrillation After Type I Flutter Ablation

Role of the Ablation Procedure

The frequent onset of atrial fibrillation early after type I flutter ablation raises concerns about a potential proarrhythmic effect of the procedure itself. The number of radiofrequency applications in this study was similar to that reported by others using similar techniques.\(^5,8,10,11,24\) We found a trend, not statistically significant, for more radiofrequency applications in patients with subsequent atrial fibrillation, similar to the findings of Philippon et al.\(^5\) In contrast, Nakagawa and colleagues\(^8\) reported that significantly more radiofrequency applications were given in patients who subsequently developed atrial fibrillation. In our patients, only right atrial enlargement was significantly associated with a greater number of radiofrequency energy applications, reflecting both greater technical difficulties and a larger area required for ablation in dilated atria. The trend toward more radiofrequency applications in patients who subsequently develop atrial fibrillation may reflect the influence of this substrate.

Large-tip catheters may produce more extensive lesions, which potentially could be proarrhythmic. The use of these catheters for ablation of type I flutter is increasing.\(^7,8,10,12\) We used 8-mm-tip catheters in 80% of study patients, but their use did not influence the subsequent risk of atrial fibrillation. The presence or absence of bidirectional isthmus conduction block at the end of the procedure also had no influence on subsequent atrial fibrillation. Finally, we found no significant differences in the determinants and clinical course of atrial fibrillation occurring early after the procedure compared with a later onset. Overall, the data from this study do not support a direct proarrhythmic effect of radiofrequency energy application in the annular isthmus, compatible with the findings of Chiang and coworkers.\(^25\)

Indirect effects related to the procedure could play a role in the early onset of atrial fibrillation in some patients. Disturbances of autonomic function are common in the initial weeks after radiofrequency ablation of the posterior septum,\(^26\) most commonly loss of parasympathetic tone. However, parasympathetic denervation associated with ablation may potentially reduce the risk of atrial fibrillation, as recently reported in an animal model autonomically mediated atrial fibrillation.\(^27\) Diminished antagonism of adrenergic tone associated with parasympathetic denervation could facilitate atrial fibrillation, particularly those with an underlying structural and electrophysiologic substrate.

Discontinuation of suppressive class I or III antiarrhythmic drugs may play a potential role in the early appearance of atrial fibrillation in some patients. However, this effect is unlikely to have been a major influence in the study population. Only 41% of patients were treated with class I or III antiarrhythmic drugs before ablation, and a history of treatment with these drugs did not predict either early or late atrial fibrillation. Only 6 patients required class I or III therapy for suppression of recurrent atrial fibrillation before the ablation procedure, and in each the drug was continued after procedure.

Relation of Type I Flutter to Atrial Fibrillation

Ambulatory monitoring in patients with atrial flutter frequently documents the coexistence of atrial fibrillation.\(^28,29\) Precise epidemiologic data regarding the prevalence of this finding are not yet available. In addition, atrial flutter may become more frequent, stable, or appear for the first time during antiarrhythmic drug therapy of atrial fibrillation.\(^28,30\) Thus the high frequency of atrial fibrillation in patients referred for type I flutter ablation (40% in the present series, and 20% to 56% of previous series\(^5,8,10,11,13,24\)) is not unexpected.

It is possible that the actual prevalence of atrial fibrillation in patients with type I flutter may be even higher, as asymptomatic episodes are more likely to be documented. Page and coworkers\(^3\) reported a high ratio of asymptomatic to symptomatic episodes in these patients.

The mechanistic relation between these 2 rhythms is incompletely defined. Waldo and Cooper\(^22\) identified atrial fibrillation as a common transitional rhythm before the onset of spontaneous type I flutter after surgical coronary revascularization. Similarly, Watson and Josephson\(^23\) reported atrial fibrillation as a frequent transitional rhythm during the induction of type I flutter by high right atrial extrastimulus testing. Roithinger et al\(^14\) examined the spontaneous conversion of atrial fibrillation to type I flutter in humans. They identified a transitional period of organized activation “streaming” in either clockwise or counterclockwise direction along the lateral and inferior annulus, which reliably predicted the onset and rotational direction of type I flutter. Atrial fibrillation was also identified as a common precursor to induced atrial flutter associated with canine sterile pericarditis.\(^24\) The transition from fibrillation to flutter was heralded by lengthening lines of functional block, permitting the emergence of a large stable reentrant circuit. These observa-
tions suggest a potentially important role for atrial fibrillation in the genesis of type I atrial flutter. In many patients, interruption of conduction through the annular–eustachian ridge isthmus may prevent the organization of atrial fibrillation into flutter. Depending on the extent of underlying structural and electrophysiological abnormalities, fibrillation may then self-terminate or persist.

In some patients, the converse relation may also exist. Atrial flutter is occasionally observed to spontaneously disorganize into atrial fibrillation in the electrophysiology laboratory. The right atrial flutter circuit is postulated to play a critical role in the initiation and maintenance of atrial fibrillation in some patients. These observations may explain the absence of recurrent fibrillation in some patients with previous documentation of this rhythm. The absence of left ventricular dysfunction and atrial enlargement may identify those patients with infrequent prior atrial fibrillation who are least likely to have symptomatic fibrillation during follow-up. However, the conclusion that such patients are no longer at risk of late atrial fibrillation may be premature until additional follow-up has accrued.

The frequent coexistence of atrial fibrillation and flutter in the study population, and the persistent risk of atrial fibrillation in a substantial number of these patients despite long-term elimination of flutter, suggest that atrial fibrillation as a trigger, rather than a consequence, of type I flutter, may be more important than previously recognized.

Limitations
Although extensive electrocardiographic documentation of symptomatic arrhythmias was available before ablation and was routinely obtained after ablation, the frequency of atrial fibrillation both before and after the procedure may be underestimated. Asymptomatic atrial arrhythmias are frequent in this population and no attempt was made to prospectively identify asymptomatic arrhythmias either before or after the procedure by systematic Holter or transtelephonic monitoring. While the study population was heterogeneous and relatively large, the total number of early and late occurrences of postablation atrial fibrillation was relatively small; it is possible that in even larger groups of patients or with longer follow-up, variables predictive of early versus late atrial fibrillation may be identified. Patients with atrial flutter who had a history of frequent atrial fibrillation were excluded from this study, and patients in whom flutter occurred while taking antiarrhythmic drugs to suppress atrial fibrillation comprised only a small minority (5%). The incidence and predictors of postablation atrial fibrillation may differ in populations with more frequent episodes of preablation atrial fibrillation.

Clinical Implications
In this study, a small group of patients with both left ventricular dysfunction and a history of atrial fibrillation (17% of the study population) were responsible for 67% of all postablation atrial fibrillation requiring long-term treatment. These findings do not necessarily imply that such patients are inappropriate candidates for catheter ablation of type I flutter. In many, atrial fibrillation was suppressed by antiarrhythmic therapy that had previously been ineffective in suppressing atrial flutter; elimination of flutter resulted in symptomatic improvement and facilitated pharmacologic control of the ventricular rate. In addition, a small number of these high-risk patients remain without atrial fibrillation and on no antiarrhythmic therapy during initial follow-up.

However, these data have important implications for management. Patients with both left ventricular dysfunction and a history of atrial fibrillation should be advised of the risk of recurrent symptoms and late atrial fibrillation. Continuation or initiation of systemic anticoagulation may be appropriate, as well as continuation of suppressive antiarrhythmic drug therapy. Some of these patients may be considered for additional ablation procedures that directly modify the substrate for further atrial fibrillation. In patients without both risk factors, a policy of observation without additional treatment appears warranted.

References


Atrial Fibrillation After Radiofrequency Ablation of Type I Atrial Flutter: Time to Onset, Determinants, and Clinical Course
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