Clinical Significance of Inducible Atrial Flutter During Pulmonary Vein Isolation in Patients With Atrial Fibrillation

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OBJECTIVES
This study was designed to determine the prevalence and clinical significance of atrial flutter (AFL) that occurs during catheter ablation for atrial fibrillation (AF).

BACKGROUND
Atrial flutter frequently occurs in patients with AF.

METHODS
Pulmonary vein isolation was performed in 133 consecutive patients (age 52 ± 11 years) for paroxysmal (n = 112) or persistent (n = 21) AF. A clinical episode of AFL was documented in 40 of the 133 patients (30%). During the ablation procedure, AFL occurred in 86 patients (65%), either spontaneously (n = 36) or by rapid atrial pacing (n = 50), with AFL being typical in the majority (80%). Cavo-tricuspid isthmus ablation was performed in 28 of the 133 patients.

RESULTS
Among the 105 patients who did not undergo isthmus ablation, 25 patients (24%) were documented to have symptomatic AFL during a mean follow-up of 609 ± 252 days. Among the clinical variables of age, gender, history of clinical AFL, ejection fraction, left atrial diameter, duration of AF, and occurrence of AFL during ablation, only a history of clinical AFL (p = 0.05) and occurrence of typical AFL during the ablation (p = 0.01) were independent predictors of symptomatic AFL during follow-up. The incidence of symptomatic AFL during follow-up was similar among patients who did and did not have long-term freedom from recurrent AF.

CONCLUSIONS
In patients with AF who have either a history of AFL or an episode of typical AFL during an electrophysiologic study, symptomatic AFL is common after pulmonary vein isolation. Therefore, cavo-tricuspid isthmus ablation is appropriate during pulmonary vein isolation if AFL has been observed clinically or in the electrophysiology laboratory. (J Am Coll Cardiol 2004;43:2057–62) © 2004 by the American College of Cardiology Foundation

Among patients with atrial fibrillation (AF) undergoing pulmonary vein (PV) isolation, inducible atrial flutter (AFL) may be encountered during the ablation procedure. However, no prior studies have investigated the prevalence or prognostic significance of inducible AFL in patients with AF. Therefore, whether inducible AFL is an appropriate indication for cavo-tricuspid isthmus ablation is unknown.

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Because premature depolarizations from PVs or episodes of AF conceivably could induce AFL, PV isolation by itself might sometimes be sufficient to eliminate recurrent episodes of AFL. However, it also is possible that patients with AF may have AFL as an independent arrhythmia.

Given these issues, the aims of this study were to determine: 1) the prevalence of AFL in patients with AF referred for a PV isolation procedure, 2) the incidence of inducible AFL during a PV isolation procedure, and 3) whether clinical AFL and/or inducible AFL is predictive of AFL after PV isolation.

METHODS

Study subjects. The subjects of this study were 133 consecutive patients with AF who underwent a PV isolation procedure with segmental ostial applications of radiofrequency (RF) energy. There were 112 men and 21 women and their mean age was 52 ± 11 years. Atrial fibrillation was paroxysmal in 112 patients and persistent in 21 patients and had been present for a mean duration of 7 ± 8 years. The mean left ventricular ejection fraction was 0.55 ± 0.04 and the mean left atrial diameter was 41 ± 4 mm. Structural heart disease was present in 25 patients (19%). Among the 133 patients, 50 were subjects of a previous study (1). Patients with a history of cavo-tricuspid isthmus ablation for AFL were not included in this study.

Study protocol. The study protocol was approved by the Institutional Review Board of the University of Michigan. A history of AFL was investigated in all patients by extensive review of all available 12-lead electrocardiograms, event monitor recordings, and 24-h Holter monitor recordings. The diagnosis of AFL was based on characteristic flutter waves.

The inducibility of AFL was determined during the PV
isolation procedures. Before catheter ablation was started, atrial pacing was performed from the coronary sinus at cycle lengths of 200 to 180 ms for 10 to 20 s at least five times. Atrial flutter was diagnosed when there were flutter waves on the surface electrocardiogram, a constant intracardiac atrial activation sequence, a cycle length of 170 to 240 ms, and <10% beat-to-beat variation in atrial cycle length. The presence of a characteristic pattern of sawtooth flutter waves in leads II, III, and aVF and positive flutter waves in lead V1 indicated that the AFL was typical. For the purposes of this study, episodes of AFL that did not meet the electrocardiographic criteria for typical AFL were classified as nontypical. Whenever possible, and in all patients who underwent cavo-tricuspid isthmus ablation, pacing was performed in the cavo-tricuspid isthmus during typical and nontypical AFLs, and the spacings interval was analyzed to determine whether the flutter was isthmus-dependent.

To minimize the probability of needing to return for a repeat ablation procedure, ablation of the isthmus was performed during the same session or within two weeks in 28 of the 133 patients (21%) who were referred from out of state and had either inducible typical flutter or a history of AFL. This was done to minimize the need for a second ablation procedure and to determine the effect of cavo-tricuspid isthmus ablation in conjunction with PV isolation on long-term freedom from recurrent AFL and AF. There was no difference in the clinical characteristics of patients who underwent an isthmus ablation and those who did not. All patients were seen in an outpatient clinic four to six weeks after the catheter ablation procedure and every three months thereafter. All patients who reported palpitations or other symptoms suggestive of an arrhythmia during follow-up were provided with an event monitor to document the cause of their symptoms. A 12-lead electrocardiogram also was obtained in all patients who had recurrent episodes of AFL to determine whether AFL was typical or nontypical.

**PV isolation.** The technique of segmental ostial ablation has been described in detail (1–3). All antiarrhythmic medications were discontinued four or five half-lives before the procedure, except for nine patients with persistent AF who were receiving amiodarone before the ablation procedure. After informed consent was obtained, we performed transeptal catheterization. Systemic anticoagulation was achieved with intravenous heparin to maintain an activated clotting time of 250 to 350 s. A deflectable decapolar catheter with a distal ring configuration (Lasso Catheter, Biosense Webster, Diamond Bar, California), and a deflectable, quadripolar 7-F catheter with 2.5-2 mm interelectrode spacing and a 4-mm distal electrode with an embedded thermistor (EP Technologies Inc., San Jose, California) were inserted into the left atrium. A quadripolar electrode catheter was positioned in the coronary sinus. Pulmonary vein isolation was performed by applications of RF energy at ostial sites that displayed a rapid PV tachycardia during AF (3,4) or that displayed PV potentials with the earliest bipolar activation and/or most rapid unipolar intrinsic deflection (5). Radiofrequency energy was applied at a target temperature of 52°C and maximum power of 30 to 35 W for 20 to 40 s. Elimination of all PV potentials and complete entrance block into PVs were the end points of ablation.

Among the 133 patients, the left superior and inferior and the right superior PVs were targeted for isolation in all patients. The right inferior PV also was targeted in 50 patients. Among the 449 targeted PVs, 440 (98%) were completely isolated with ostial applications of RF energy.

After the procedure, all patients were anticoagulated with intravenous heparin for 12 to 18 h, then discharged and treated with low-molecular-weight heparin for four to five days and warfarin for at least six weeks.

A repeat PV isolation procedure was performed in 34 of 133 patients (25%) who had recurrent episodes of AF after the first procedure. In all of these patients there was recovery of conduction over a previously ablated PV fascicle in at least one PV.

**RF catheter ablation of AFL.** The RF catheter ablation of the cavo-tricuspid isthmus was performed during pacing from the coronary sinus or during AFL by delivering contiguous 45- to 60-s applications of RF energy along the isthmus (6–8). The RF energy was delivered with a conventional 4-mm tip ablation catheter with a target temperature of 60°C and a maximum power output of 50 W. A reversal in the atrial activation sequence along the lateral right atrial wall and a parallel corridor of double potentials along the ablation line with a double-potential interval >110 ms during coronary sinus pacing indicated complete conduction block in the isthmus (7,8).

**Statistical analysis.** Continuous variables are expressed as mean ± SD. Continuous variables were compared with Student’s t test. Categorical variables were compared with the chi-square test. Multivariate logistic regression analyses were performed to determine the predictors of inducibility, and recurrent episodes of AFL after a PV isolation procedure. Kaplan–Meier analysis with the log-rank test was performed to determine freedom from recurrent AFL in patients who did and did not have an episode of inducible AFL. A value of p < 0.05 indicated statistical significance.

**RESULTS**

**Prevalence of AFL before PV isolation.** Among the 133 patients with AF, 40 (30%) had a documented episode of AFL before the PV isolation procedure. Among the clinical variables of age, gender, duration of AF, whether AF was
paroxysmal or persistent, left ventricular ejection fraction, left atrial diameter, and presence of structural heart disease, none was significantly associated with a history of AFL (Table 1). In addition, there was no difference in the number of electrocardiographic tracings available for review between the patients with and without a history of AFL.

**AFL during PV isolation.** During the PV isolation procedure, an episode of AFL occurred in 86 of the 133 patients (65%). Among the 86 patients, 68 (79%) had typical AFL, and 18 (21%) had nontypical AFL. Both typical and nontypical AFL occurred in four of these patients. The mean cycle lengths of the typical and nontypical AFLs were 234 ± 29 ms and 235 ± 33 ms, respectively (p = 0.9).

Among the clinical variables of age, gender, a history of AFL, whether AF was paroxysmal or persistent, duration of AF, structural heart disease, left ventricular ejection fraction, left atrial size, and occurrence of typical or nontypical AFL during the electrophysiologic study, only a history of AFL predicted the occurrence of AFL during the electrophysiologic study (p = 0.03, Table 2).

**Mode of initiation and termination of AFL.** Among the 86 patients with AFL during the PV isolation procedure, the flutter occurred spontaneously in 4 patients (5%), was induced by rapid atrial pacing in 50 patients (58%), and was induced by an episode of AF in 32 patients (37%). There was no relationship between the mode of onset of AFL and whether the flutter was typical or nontypical. Among the 86 patients, AFL terminated spontaneously within 2.1 ± 3.9 min in 25 patients (29%). Among the 61 patients with sustained AFL, rapid atrial pacing resulted in restoration of sinus rhythm in 12 patients (20%) and AF in 40 patients (65%), and sinus rhythm was restored during RF catheter ablation of the cavo-tricuspid isthmus in the remaining nine patients (15%).

**Cavo-tricuspid isthmus ablation.** Cavo-tricuspid isthmus ablation was performed in 28 of the 133 patients (21%) who had either a documented history of AFL (n = 17) or an episode of AFL during the PV isolation procedure (n = 11). Complete bidirectional conduction block was achieved in all patients.

**Recurrence of AFL and AF after PV isolation.** During a mean follow-up of 609 ± 252 days, 55 of the 105 patients (52%) who did not undergo cavo-tricuspid isthmus ablation in conjunction with PV isolation experienced recurrent palpitations. Among these 55 patients, the symptomatic episodes were caused by AF in 30 patients (54%), AFL in 13 patients (24%), and both AF and AFL in 12 patients (22%). Among the 25 recurrent episodes of AFL, 24 were typical and 1 was nontypical.

**Predictors of AF during follow-up.** In 105 patients with AF who did not undergo cavo-tricuspid isthmus ablation, among the variables of age, gender, a history of AFL, whether AF was paroxysmal or persistent, duration of AF, presence of structural heart disease, left ventricular ejection fraction, left atrial size, and occurrence of typical or nontypical AFL during the electrophysiologic study, only a history of AFL (p = 0.05) and the occurrence of an episode of typical AFL during PV isolation (p = 0.01) (Fig. 1) were independent predictors of symptomatic AFL during follow-up (univariate analysis is shown in Table 3). The positive and negative predictive values of inducible AFL for symptomatic AFL during follow-up were 37% and 88%, respectively (p = 0.004, odds ratio = 4.1, 95% confidence interval = 1.5 to 10.9).

**Efficacy of PV isolation and recurrence of AFL.** Among the 105 patients who did not undergo cavo-tricuspid isthmus ablation, symptomatic AFL occurred during follow-up in 13 of the 63 patients (21%) who were free from recurrent episodes of AF and in 12 of the 42 patients (29%) who had recurrent AF (p = 0.4). None of the 28 patients who underwent cavo-tricuspid isthmus ablation had symptomatic AFL during follow-up.

Atrial fibrillation occurred in 6 of the 28 patients (21%) who underwent cavo-tricuspid isthmus ablation and in 42 of the 105 patients (40%) who did not (p = 0.07).

**Ablation of AFL.** Among the 25 patients who had symptomatic AFL during follow-up, an ablation procedure aimed at elimination of the flutter was performed in 22 of 24 patients with typical AFL and in 1 patient with nontypical AFL at a mean of 163 ± 90 days after the PV isolation procedure. Complete bidirectional isthmus conduction

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### Table 1. Clinical Characteristics of Patients With and Without a History of AFL

<table>
<thead>
<tr>
<th></th>
<th>History of AFL (n = 40)</th>
<th>No History of AFL (n = 93)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male/female)</td>
<td>33/7</td>
<td>79/4</td>
<td>0.7</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>50 ± 13</td>
<td>52 ± 10</td>
<td>0.3</td>
</tr>
<tr>
<td>AF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>37 (92%)</td>
<td>75 (81%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Persistent</td>
<td>3 (8%)</td>
<td>18 (19%)</td>
<td></td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>6 (15%)</td>
<td>19 (20%)</td>
<td>0.4</td>
</tr>
<tr>
<td>LV EF</td>
<td>0.55 ± 0.05</td>
<td>0.55 ± 0.04</td>
<td>0.4</td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>40 ± 4</td>
<td>41 ± 4</td>
<td>0.4</td>
</tr>
<tr>
<td>Duration of AF (yrs)</td>
<td>7 ± 8</td>
<td>7 ± 8</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Data are shown as mean ± SD. AF = atrial fibrillation; AFL = atrial flutter; EF = ejection fraction; LV = left ventricular.

### Table 2. Comparison of Patients With and Without AFL During Catheter Ablation to Isolate the Pulmonary Veins

<table>
<thead>
<tr>
<th></th>
<th>AFL (n = 86)</th>
<th>No AFL (n = 47)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male/female)</td>
<td>75/11</td>
<td>37/10</td>
<td>0.3</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>53 ± 11</td>
<td>49 ± 10</td>
<td>0.1</td>
</tr>
<tr>
<td>Typical AFL</td>
<td>68 (79%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nontypical AFL</td>
<td>18 (21%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>74 (86%)</td>
<td>38 (80%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Persistent AF</td>
<td>12 (14%)</td>
<td>9 (20%)</td>
<td></td>
</tr>
<tr>
<td>Duration of AF (yrs)</td>
<td>8 ± 8</td>
<td>7 ± 6</td>
<td>0.4</td>
</tr>
<tr>
<td>History of AFL</td>
<td>32 (37%)</td>
<td>8 (17%)</td>
<td>0.03</td>
</tr>
<tr>
<td>LV EF</td>
<td>0.55 ± 0.04</td>
<td>0.53 ± 0.05</td>
<td>0.2</td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>41 ± 4</td>
<td>41 ± 4</td>
<td>0.4</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>18 (21%)</td>
<td>7 (15%)</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Data are shown as mean ± SD. Abbreviations as in Table 1.
block was achieved in each of the 22 patients with typical AFL, and a left AFL was successfully ablated in the 1 patient who had nontypical AFL.

**Long-term freedom from symptomatic AFL and AF.** At a mean follow-up of 609 ± 252 days, 83 of the 133 (62%) patients were free from recurrent episodes of AFL and AF in the absence of any antiarrhythmic drug therapy.

**DISCUSSION**

**Main findings.** The main findings of this study are the following: 1) AFL occurs in at least one-third of patients with AF; 2) AFL, usually induced either by atrial pacing or by AF, may be observed in two-thirds of patients undergoing PV isolation for AF, and ~80% of these episodes are typical AFL; 3) the occurrence of typical AFL during a PV procedure is predictive of symptomatic AFL during follow-up after PV isolation; and 4) the successful elimination of symptomatic AF by PV isolation is not associated with freedom from symptomatic AFL.

These findings imply that it is appropriate to ablate the cavo-tricuspid isthmus whenever typical AFL is observed in the course of a catheter ablation procedure aimed at elimination of AF.

**Prevalence of AFL in patients with AF.** In this study, AFL occurred in more than one-third of patients with AF. Because only documented episodes of AFL were included in this study, and because electrocardiographic documentation of every symptomatic episode of supraventricular tachycardia was not available, the true prevalence of AFL in patients with AF probably was underestimated.

The reasons that AF and AFL often occur in the same patient are unclear. It may be that the same premature depolarizations that trigger AF also trigger AFL. Alternatively, some episodes of AF may organize into AFL, either...
spontaneously or because of a drug effect (9,10). Atrial fibrillation may promote the formation of intercaval block in the right atrium, which may be critical for the initiation of AFL (11,12). It is also possible that at least some episodes of AFL may degenerate into AF (12,13). Atrial flutter with a short cycle length may result in fibrillatory conduction (11). Moreover, the electrophysiologic and/or structural remodeling that accompanies AF may promote the occurrence of AFL, or vice versa (14,15).

Although this study does not establish the mechanisms by which AF and AFL coexist in the same patient, it does provide some relevant observations. The fact that symptomatic AFL during follow-up was independent of whether or not AF was successfully eliminated by PV isolation suggests that the occurrence of AFL in the patients in this study may not have depended on triggers originating in the PVs or on induction by AF. However, brief episodes of AF that otherwise would have been asymptomatic may have induced AFL in some patients. Therefore, firm conclusions regarding the mechanism of AFL after PV isolation are not possible and require further study.

**Inducibility of AFL.** At least one episode of AFL was observed in two-thirds of patients during a catheter ablation procedure to isolate the PVs. Thus, AFL occurred in the electrophysiology laboratory in many patients in whom a clinical episode of AFL never had been documented. It is possible that AFL observed in the electrophysiology laboratory sometimes is a nonspecific finding. However, in a prior study, AFL was inducible in only 36% of patients with no history of AFL or supraventricular tachycardia during an electrophysiologic study, whereas it was easily inducible in 92% of patients with a history of AFL (16). Therefore, the occurrence of AFL in the electrophysiology laboratory may have identified patients in this study who had experienced AFL that never had been documented.

Typical AFL was four times more likely to be observed in the electrophysiology laboratory than nontypical AFL. Although the inducibility of typical AFL was predictive of symptomatic AFL during follow-up after PV isolation, the inducibility of nontypical AFL was not predictive of any future symptomatic events. Therefore, it may not be necessary to ablate nontypical AFL in patients undergoing PV isolation for AF.

**Cavo-tricuspid isthmus ablation and recurrence of AF.** There was a trend toward a lower incidence of recurrent AF after PV isolation in patients who underwent cavo-tricuspid isthmus ablation than in those who did not. This suggests that AFL may have been responsible for some episodes of AF. Consistent with a facilitatory role of typical AFL in the pathogenesis of AF, several prior studies have demonstrated that the incidence of AF may be lower after ablation of the cavo-tricuspid isthmus (17–20). However, in none of these prior studies was the role of PV isolation assessed.

**Study limitations.** A limitation of this study is that episodes of AFL were classified as typical or nontypical based on analysis of flutter-wave morphology on the electrocardiogram. Therefore, some of the AFLs classified as nontypical may have in fact been clockwise isthmus-dependent flutter. However, because clockwise isthmus-dependent AFL constitutes only ~15% of all episodes of isthmus-dependent AFL (21), this probably was not a source of large error.

Another limitation is that cavo-tricuspid isthmus ablation was performed in conjunction with PV isolation in some patients. To most accurately determine the prognostic significance of spontaneous or induced AFL, isthmus ablation would not have been performed in any patients.

A third limitation is that asymptomatic episodes of AFL may not have been captured during follow-up. However, documenting asymptomatic episodes of AFL would have required continuous monitoring for extended periods of time, which was not feasible in the present study.

**Conclusions.** Atrial flutter, whether spontaneous, induced by atrial pacing, or by an episode of AF, often is observed in patients undergoing a catheter ablation procedure aimed at elimination of AF. Because the occurrence of typical AFL during a catheter ablation procedure is predictive of symptomatic AFL during follow-up, catheter ablation of the cavo-tricuspid isthmus should be considered in conjunction with PV isolation to avoid the need for a second catheter ablation procedure. The reasons that AFL and AF often coexist in the same patient remain to be determined in future studies.

**REFERENCES**


