Perception of Atrial Fibrillation Before and After Radiofrequency Catheter Ablation

Relevance of Asymptomatic Arrhythmia Recurrence

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Background—The objective of this study was to assess the incidence and impact of asymptomatic arrhythmia in patients with highly symptomatic atrial fibrillation (AF) who qualified for radiofrequency (RF) catheter ablation.

Methods and Results—In this prospective study, 114 patients with at least 3 documented AF episodes together with corresponding symptoms and an ineffective trial of at least 1 antiarrhythmic drug were selected for RF ablation. With the use of CARTO, circumferential lesions around the pulmonary veins and linear lesions at the roof of the left atrium and along the left atrial isthmus were placed. A continuous, 7-day, Holter session was recorded before ablation, right after ablation, and after 3, 6, and 12 months of follow-up. During each 7-day Holter monitoring, the patients recorded quality and duration of any complaints by using a detailed symptom log. More than 70 000 hours of ECG recording were analyzed. In the 7-day Holter records before ablation, 92 of 114 patients (81%) had documented AF episodes. All episodes were symptomatic in 35 patients (38%). In 52 patients (57%), both symptomatic and asymptomatic episodes were recorded, whereas in 5 patients (5%), all documented AF episodes were asymptomatic. After ablation, the percentage of patients with only asymptomatic AF recurrences increased to 37% (P<0.05) at the 6-month follow-up. An analysis of patient characteristics and arrhythmia patterns failed to identify a specific subset who were at high risk for the development of asymptomatic AF.

Conclusions—Even in patients presenting with highly symptomatic AF, asymptomatic episodes may occur and significantly increase after catheter ablation. A symptom-only–based follow-up would substantially overestimate the success rate. Objective measures such as long-term Holter monitoring are needed to identify asymptomatic AF recurrences after ablation. (Circulation. 2005;112:307-313.)

Key Words: atrium ■ ablation ■ arrhythmia ■ fibrillation ■ follow-up studies

Asymptomatic or silent arrhythmia is a frequent condition in patients with atrial fibrillation (AF). The prevalence of asymptomatic AF found incidentally on clinical examination is ≈20%. Studies with transtelephonic arrhythmia monitoring or implantable monitoring devices have reported asymptomatic AF in up to 50% of patients evaluated. The patient cohorts observed in most of these studies participated in population surveys such as the Framingham Study, in antiarrhythmic drug trials, or in instances where monitoring followed pacemaker implantation for sinus node dysfunction or atrioventricular block. The incidence of asymptomatic arrhythmia in patients presenting with highly symptomatic AF who qualified for radiofrequency (RF) catheter ablation is unknown. Because AF catheter ablation is a new and potentially curative therapy and is currently performed in an increasing number of patients, data on asymptomatic AF in this subset of patients may have important implications for the overall success rate as well as for the individual patient with regard to concomitant medical therapy, eg, oral anticoagulation. Thus, the present prospective study aimed to evaluate AF recurrences, particularly asymptomatic ones, in patients undergoing RF catheter ablation by repetitive, continuous, digital, long-term Holter ECGs.

Methods

Patient Selection and Characteristics

One hundred fourteen patients (81 men, 33 women; mean±SD age, 54±9 years) with highly symptomatic AF were included in this prospective study. Inclusion criteria were a history of AF >18 months, previously ineffective antiarrhythmic drug therapy (at least 1 antiarrhythmic drug), and at least 3 documented AF episodes together with corresponding symptoms. Before inclusion into the study, patients judged their overall impairment due to the arrhythmia on an ordinal scale between 0 and 10 (0 being no complaints at all and 10 being unbearable complaints). Most (95%) patients with documented AF during the 7-day ECG period described their individual impairment due to the arrhythmia as medium to severe on that ordinal scale (≥6).

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ECG Monitoring and Follow-Up

After inclusion into the study and before ablation, a continuous 7-day ECG (LifeCard CF, Delmar Reynolds Medical Inc) was recorded in all patients. The patients were equipped with a detailed symptom log and instructed on how to document duration and quality of any occurring symptoms. Complaints of palpitations, dyspnea, dizziness, and chest pain were taken as surrogates of AF. The continuous 7-day ECG was repeated immediately after ablation and after 3, 6, and 12 months of follow-up. In cases when symptoms occurred outside the recording periods, patients were advised to contact our institution or the referring physician to obtain ECG documentation. AF >30 seconds was considered an episode of sustained AF recurrence. Recordings of atrial flutter were analyzed separately.

A total of 114 patients were included in the study in a consecutive fashion. All patients have completed at least 3 months of follow-up. At the time of data analysis, 110 patients had completed at least 6 months of follow-up after the ablation procedure. Two patients were lost to follow-up within the first 6 months after ablation. Thus, data obtained for 108 patients were analyzed at 6 months. Of these 108 patients, 10 (8.8%) with recurrences of AF underwent a reablation procedure, and 2 additional patients were lost to follow-up within the monitoring period from 6 months to 1 year. Seventy patients have completed 1 year of follow-up, whereas 26 patients are currently in follow-up between 6 months and 1 year. Thus, the dropout rate was low during the total course of the study. We lost 4 patients (3.5%) during follow-up, and 10 patients (8.8%) did not complete 1 year of follow-up because of a reablation after 6 months.

Data Analysis

More than 70,000 hours of continuous ECG recording were analyzed. The physician performing the analysis was blinded with regard to patient name, date of ablation, and the patient’s symptom log. After symptoms and rhythms were correlated, the 7-day ECG was divided into hours with symptomatic AF, hours with asymptomatic AF, hours with symptomatic sinus rhythm (SR), and hours with asymptomatic SR. Furthermore, the single AF episode was classified as symptomatic or asymptomatic. Because of the difficulty in discriminating the symptomaticity in cases of multiple, short episodes (<30 minutes) separated by only a few minutes of SR, these episodes together were considered a single episode. Finally, the patients with documented AF were divided into 3 different groups of AF perception: symptomatic patients only, asymptomatic patients only, and patients with a mixture of symptomatic and asymptomatic AF.

Statistics

Continuous variables are presented as mean±SD, where appropriate. In cases of a non-gaussian distribution, medians and quartiles are given. Categorical variables are expressed as numbers and percentages of patients. During follow-up, the changes in the number of patients within the 3 AF perception groups as well as other categorical data, such as the number of patients taking β-blocker and antiarrhythmic drugs, were tested for any statistically significant difference with the χ²-test for trend. When a significant difference was found, each follow-up point was tested individually against status before ablation with the McNemar test.

Changes in continuous data during follow-up, such as total AF hours (ie, AF duration), total AF episodes, percentage of asymptomatic AF hours and percentage of asymptomatic AF episodes, mean heart rate during AF, and mean heart rate during SR, were tested for any statistically significant difference with Friedman’s test. When a significant difference was found, each follow-up point was tested individually against status before ablation by the Wilcoxon test and a Bonferroni correction. Additionally, the change in the percentage of asymptomatic AF hours and the percentage of asymptomatic AF episodes throughout follow-up was analyzed with the χ² test for trend in binomial proportions (the 2 groups consisting of patients either with or without an increase of asymptomatic AF hours or AF episodes).

To compare the characteristics of patients within the 3 different AF perception groups, continuous data such as age, duration of AF history, AF burden (episodes and hours), mean heart rate during AF, mean heart rate during SR, and echocardiographic parameters were tested for any statistically significant difference with a 1-way ANOVA for normally distributed data and the Kruskal-Wallis test for data in a non-gaussian distribution. Differences in categorical data, such as sex, presence of structural heart disease, previous ablation attempts, and use of β-blocker and antiarrhythmic drugs, were tested for statistical significance among each of the 3 perception groups with the χ² test. A probability value <0.05 was considered statistically significant.

Results

Rhythm Analysis

The results are shown in Table 1. During the entire course of the study, the percentage of patients with asymptomatic AF...
only in all patients with documented AF recurrences significantly increased from 5% at baseline to 22% after ablation ($P<0.027$), to 38% at 3-month follow-up ($P=0.021$), 37% at 6-month follow-up ($P=0.021$), and 36% at 12-month follow-up ($P=0.05$).

### Change in AF Characteristics

During the 7-day ECG periods, patients with AF showed a median of 1 (1, 3) AF episodes before ablation compared with 2 (1, 5) AF episodes immediately after ablation ($P=0.1$), 2 (1, 6) after 3 months ($P=0.07$), 2 (1, 4) after 6 months ($P=0.16$), and 2 (1, 5) after 12 months ($P=0.11$) (Figure 1). The median percentage of asymptomatic AF episodes increased from 0% (0%, 25%) before ablation to 50% (0%, 89%) immediately after ablation ($P=0.001$), 50% (0%, 100%) after 3 months ($P=0.004$), 50% (0%, 100%) after 6 months ($P=0.017$), and 58% (0%, 100%) after 12 months ($P=0.04$) (Figure 1).

For patients with documented AF, the median total arrhythmia duration during the 7-day ECG periods measured 38 (10, 133) hours before ablation and postinterventionally declined to 36 (22, 79) hours immediately after ablation ($P=0.21$), 23 (8, 41) hours after 3 months ($P=0.023$), 17 (8, 43) hours after 6 months ($P=0.038$), and 10 (3, 25) hours after 12 months ($P=0.013$) (Figure 2). The percentage of asymptomatic AF among the total arrhythmia duration showed a trend to increase nonsignificantly, from 62% (6%, 88%) before ablation, 70% (10%, 98%) immediately after ablation ($P=0.13$), 73% (23%, 96%) after 3 months ($P=0.18$), 77% (8%, 100%) after 6 months ($P=0.15$), and 77% (34%, 88%) after 12 months ($P=0.85$) (Figure 2).

The observed decrease in total AF duration after RF ablation resulted in a marked change in the AF distribution/variability pattern during the 7-day recording periods. Figure 3 illustrates the percentage of patients with documented AF during 1 to 7 days of the Holter recording period. Before ablation, 40% of patients with AF showed arrhythmias during a single day of the 7-day period only. Twelve months after ablation, 74% of patients with recurrences showed AF during a single day of the 7-day period only, and furthermore, none of the patients with AF recurrences had an arrhythmia on >3 days of the 7-day period (Figure 3).

### Role of β-Blocker and Antiarrhythmic Drugs

As part of our study protocol, after ablation, the patients received a β-blocker and an antiarrhythmic drug (flecainide or amiodarone) for at least 3 months, if tolerated. Afterward, the medication was adapted on an individual basis. Table 2

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**Figure 1.** Left, Box-and-whisker plot showing number of AF episodes recorded during 7-day Holter ECG monitoring in patients with documented AF occurrences before and after RF ablation (abl.). Medians, quartiles, and extreme values are given. Right, Box-and-whisker plot showing percentage of asymptomatic AF episodes among all documented AF episodes. Medians, quartiles, and extreme values are given. Change in number of AF episodes during follow-up ($P=0.34$) and increase in percentage of asymptomatic episodes ($P=0.04$) were tested for any significant difference with Friedman’s test. In post hoc analysis, each follow-up point was tested against before ablation with Wilcoxon’s test and Bonferroni correction. *$P<0.05$.

**Figure 2.** Left, Box-and-whisker plot showing hours of AF (ie, total AF duration) recorded during 7-day Holter ECG monitoring in patients with documented AF occurrences before and after RF ablation (abl.). Medians, quartiles, and extreme values are given. Right, Box-and-whisker plot showing percentage of asymptomatic hours among all documented AF hours. Medians, quartiles, and extreme values are given. Decrease in total AF duration after ablation ($P=0.001$) and change in percentage of asymptomatic hours ($P=0.07$) were tested for any significant difference with Friedman’s test. In post hoc analysis, each follow-up point was tested against before ablation with Wilcoxon’s test and Bonferroni correction. *$P<0.05$.
summarizes the medications for patients with documented AF recurrences during follow-up. Because of the study protocol, the percentage of patients taking β-blockers increased from 57% before ablation to 77% after ablation, 86% after 3 months, 70% after 6 months, and 72% after 12 months. The increase after ablation (P = 0.013) and after 3 months (P = 0.012) was statistically significant (Table 2).

The use of class Ic antiarrhythmic drugs significantly decreased after the 3-month follow-up, from 51% before ablation to 24% after 12 months (P = 0.001). The percentage of patients taking class III antiarrhythmic drugs steadily declined from 41% before ablation to 16% after 12 months (P = 0.001) (Table 2).

Comparing the intake of β-blockers and/or antiarrhythmic drugs among the 3 different AF-perception groups did not

| TABLE 2. Use of β-Blockers and Antiarrhythmic Drugs, Mean Heart Rate During AF, and Mean Heart Rate During SR in Patients With AF |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Before Ablation | After Ablation  | 3 Months        | 6 Months        | 12 Months       |
| No. of patients with AF | 92 (81%)        | 78 (68%)        | 49 (43%)        | 54 (50%)        | 25 (36%)        |
| β-Blockers       | 57%             | 77%             | 86% P = 0.013   | 70% P = 0.14    | 72% P = 0.1       |
| Class Ic antiarrhythmics | 51%             | 58%             | 51% P = 0.51    | 35% P = 0.014   | 24% P = 0.001    |
| Class III antiarrhythmics | 41%             | 23%             | 30% P = 0.08    | 16% P = 0.001   | 16% P = 0.001    |
| AF-HR (25th, 75th percentile) | 110 (95, 120)   | 100 (90, 120)  | 100 (91, 120)  | 110 (90, 120)  | 110 (90, 130)    |
| SR-HR (25th, 75th percentile) | 66 (60, 75)     | 66 (60, 72)    | 65 (60, 72)    | 65 (56, 74)    | 70 (59, 74)    |

HR indicates heart rate.
show a significant difference at any time before or after ablation.

### Role of Heart Rate During AF

Table 2 displays the mean heart rate during AF after RF ablation among all patients with documented arrhythmia recurrences. Medians and quartiles are given. Despite the postinterventional increase in asymptomatic AF and at least a temporary increase in β-blocker medication, the mean heart rate during the arrhythmia did not change significantly (110 bpm before ablation, 100 bpm after ablation, and 100, 110, and 110 bpm after 3, 6, and 12 months, respectively [Table 2]).

Furthermore, the mean heart rate during AF was compared among patients with different AF perception (symptomatic patients only, asymptomatic patients only, and symptomatic+asymptomatic patients) at each follow-up point before and after RF ablation. Corresponding to the comparable usage of β-blocker and antiarrhythmic medications among these 3 groups, mean heart rate during AF was not significantly different at any follow-up point.

### Role of Patient Characteristics

To analyze other parameters possibly influencing arrhythmia perception, characteristics of patients with different AF perception (symptomatic patients only, asymptomatic patients only, and symptomatic+asymptomatic patients) were compared among these 3 groups. No statistically significant differences with respect to age, sex, left ventricular ejection fraction, left atrial size, left atrial appendage flow velocity, and duration of AF history were found. The majority of patients in all 3 groups experienced paroxysmal AF (91% versus 80% versus 81%, $P=0.21$) and had no structural heart disease (91% versus 100% versus 82%, $P=0.12$). In all 3 groups, previous AF catheter ablation had been similar (12% versus 20% versus 15%, $P=0.15$). Though statistically not significant, in patients with asymptomatic AF a tendency toward a longer AF duration during the 7-day ECG period before ablation was observed (19 versus 39 versus 31 hours, $P=0.07$). A possible influence of socioeconomic factors on the perception of AF was studied by analyzing the percentage of university graduates in all 3 groups. However, no significant difference could be found. In summary, none of the studied parameters was significantly different and thereby predictive for the perception of AF.

### Occurrence and Perception of Atrial Flutter

The number of patients with documented atrial flutter during the 7-day ECG periods was 9 (7.8%) patients before ablation, 14 (12.3%) immediately after ablation, and 6 (5.5%), and 1 (1.4%) patients after 3, 6, and 12 months, respectively (Table 3). All patients with atrial flutter showed episodes of AF on the same 7-day ECG as well.

Throughout the study, only 2 (1.7%) patients before ablation and 2 patients (1.7%) immediately after ablation recognized every episode of atrial flutter. At 3, 6, and 12 months’ follow-up, the arrhythmia was always at least partially asymptomatic (Table 3). A comparison of the mean heart rate between symptomatic and asymptomatic episodes of atrial flutter revealed a significant difference, with asymptomatic episodes showing a lower mean heart rate (125 versus 95 bpm, $P=0.04$) (Figure 4). These results indicate that in cases of a near to normal ventricular rate, recurrences of atypical
atrial flutter after an AF ablation procedure could be more asymptomatic than AF recurrences themselves. However, the limited number of patients with atrial flutter at each follow-up point precluded a more detailed analysis of arrhythmia pattern and patient characteristics influencing arrhythmia perception.

**Discussion**

**Main Findings of the Study**

The results of this study show that asymptomatic AF can occur in patients presenting with highly symptomatic AF who qualify for catheter ablation. Before ablation, >50% of patients showed a mixture of symptomatic and asymptomatic AF, whereas only 38% of patients recognized all AF episodes accurately. Moreover, 5% of patients had only asymptomatic AF during the initial 7-day ECG period, despite previously documented symptomatic AF episodes. After catheter ablation, the incidence of asymptomatic AF significantly increased: At 3, 6, and 12 months’ follow-up, 38%, 37%, and 36% of patients with arrhythmia recurrences were completely asymptomatic. These findings may have important implications for strategy and the intensity of follow-up after catheter ablation procedures.

**Perception of AF Before Catheter Ablation**

Patients selected for AF catheter ablation represent a highly symptomatic subgroup within the total AF population. However, the detailed arrhythmia characteristics of these patients with respect to symptomatic and asymptomatic AF episodes have not been described before. In the present study, >95% of patients with documented AF during the 7-day Holter period before ablation showed symptomatic AF episodes, characterizing a population of truly highly symptomatic individuals. On the other hand, >50% of them also had asymptomatic episodes, a surprisingly high number. For a similar patient cohort, no comparable data are available in the literature. It may be argued that our patient population was not representative of AF patients selected for catheter ablation in general. However, by comparing the patient characteristics in this analysis with data from other studies on AF catheter ablation, no striking differences could be found.

**Perception of AF After Catheter Ablation**

The significant increase in patients with asymptomatic AF only after the ablation procedure may be discussed in different ways. First, the percentage of patients taking β-blockers significantly increased after ablation because of our study protocol, which recommends β-blockers to all patients undergoing the procedure. That increase in β-blocker use may explain the increase in asymptomatic-only patients directly after ablation. However, during further follow-up, the percentage of patients taking β-blockers remained stable, and the percentage of patients taking antiarrhythmic drugs significantly decreased. Thus, despite a reduction in antiarrhythmic drug use, the percentage of completely asymptomatic patients increased, making a causal relation between drugs and symptoms in our patient population unlikely. Moreover, the mean heart rate during AF was not significantly different between symptomatic and asymptomatic patients.

Invasive treatment of AF per se may result in changes of arrhythmia perception caused by (1) a placebo effect, (2) an ablation-induced change in arrhythmia pattern, or (3) an ablation-induced modulation of the autonomic nervous system. In nonrandomized and nonblinded studies such as the present one, the impact of the placebo effect on the perception of AF is difficult to estimate. From other invasive procedures such as percutaneous myocardial laser revascularization, it is well known that simply the fact of an invasive procedure being performed significantly alters the perception of preexisting symptoms. The same may also be true after catheter ablation of AF. Gerstenfeld et al and Berkowitsch et al reported an improved quality of life despite AF recurrences after pulmonary vein disconnection procedures, which supports that hypothesis. Circumferential pulmonary vein ablation may change the arrhythmia pattern and characteristics. Details about rhythm outcome and changes in arrhythmia pattern observed in our patients are presented elsewhere. As a general pattern, in cases of postinterventional arrhythmia recurrences, the number of AF episodes was unchanged, but the duration of single episodes decreased. However, comparing the arrhythmia pattern (AF duration, number of AF episodes, mean heart rate) in patients with and without symptoms did not reveal any significant difference, not even a trend. Thus, as observed in other studies of asymptomatic AF, it is impossible to define a subset of patients who might be preserved from asymptomatic arrhythmias. Furthermore, results of the present study as well as previously published data show that a history of symptomatic AF does not guarantee only symptomatic recurrences in the future. Eventually, the effects of circumferential pulmonary vein ablation on the autonomic nervous system of the heart, though currently not completely understood, may have an impact on the perception of AF after ablation. Further studies are needed to clarify this issue.

In a recent study, Oral et al described the prevalence of symptomatic and asymptomatic AF after an apparently successful segmental pulmonary vein disconnection procedure in 60 of 244 consecutive patients. For 30 days, they were provided with a patient-activated transtelephonic event recorder 642±195 days after the ablation procedure. All 60 patients had not had an episode of symptomatic AF at 6 months after the ablation procedure until participating in that follow-up study. AF was documented in 8 of 60 patients (13%) and was symptomatic in 7 patients but asymptomatic in only 1. The authors concluded that asymptomatic AF episodes are infrequent after apparently successful catheter ablation procedures. The data presented by Oral et al may be interpreted as inconsistent with the findings of our study. However, this may at least in part be due to significant differences in study protocols. The most important differences include patient selection (voluntary subset of 60 of 244 patients selected almost 2 years after ablation versus 114 consecutive patients prospectively included in our study), ablation strategy (segmental pulmonary vein disconnection versus circumferential left atrial ablation in our study), the time frame of follow-up (almost 2 years after ablation versus the first 12 months after ablation in our study), as well as the rhythm monitoring strategy (event recorders versus continu-
ous long-term Holter recordings). When comparing the results of the study by Oral et al with our data, the important methodological limitations of their study must be considered, which have also been addressed in detail in an editorial published along with their article. One interesting and unanswered question about the data from Oral et al relates to the fact that 12% of patients who were completely free of symptomatic AF recurrences from 6 months to almost 2 years after the ablation procedure suddenly developed symptomatic AF recurrences within a mean of only 25 days of follow-up after having been equipped with an event recorder. One possible explanation may be that the patients did have asymptomatic AF after the ablation procedure and were simply sensitized to arrhythmia-related symptoms by participating in a scientific study. However, this is only speculative. Overall, the discrepant results obtained in both studies underline the need for additional detailed studies to further clarify the relevance of asymptomatic AF recurrences after catheter ablation procedures.

Study Limitations
Possible limitations of the present study are related to the high percentage of patients taking β-blocker and antiarrhythmic drugs after ablation (discussed earlier in detail). Therefore, it cannot be excluded that more restrictive use of these drugs might have resulted in a lower incidence of asymptomatic AF.

Clinical Implications
The results of our study show that asymptomatic AF frequently occurs in highly symptomatic patients before and after RF catheter ablation. As a consequence, close and objective follow-up strategies with repetitive, long-term, Holter monitoring devices are necessary to analyze rhythm outcome after these procedures. Moreover, our data show that a symptom-only–based follow-up could substantially overestimate the success rate of the ablation procedure. In that sense, our analysis may help explain the inconsistent data on the success rates of AF catheter ablation reported in the literature. For the individual patient, the most significant implication of asymptomatic AF is related to the need for oral anticoagulation after the ablation procedure. Thus, withdrawal of oral anticoagulation after ablation should be considered carefully, based on reliable and objective measures such as long-term Holter records rather than symptoms.

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