Discerning the Incidence of Symptomatic and Asymptomatic Episodes of Atrial Fibrillation Before and After Catheter Ablation (DISCERN AF)

A Prospective, Multicenter Study

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Background: The DISCERN AF study (Discerning Symptomatic and Asymptomatic Episodes Pre and Post Radiofrequency Ablation of Atrial Fibrillation) monitored atrial fibrillation (AF) using an implantable cardiac monitor (ICM) to assess the incidence and predictors of asymptomatic AF before and after catheter ablation.

Methods: Patients with symptomatic AF underwent implantation of an ICM with an automated AF detection algorithm 3 months before and 18 months after ablation. Patients kept a standardized diary to record symptoms of arrhythmia, and ICM data were downloaded every 3 months. All episodes were blindly adjudicated and correlated with the diary. Asymptomatic recurrences were ICM episodes of 2 minutes or longer with no associated diary symptoms.

Results: Fifty patients had 2355 ICM episodes. Of these, 69.0% were true AF/atrial flutter (AFL)/atrial tachycardia (AT); 16.0%, sinus with extrasystoles; 11.0%, artifact; and 4.0%, sinus arrhythmia. Total AF/AFL/AT burden was reduced by 86% from a mean (SD) of 2.0 (0.5) h/d per patient before to 0.3 (0.2) h/d per patient after ablation ($P<.001$), and 56.0% of all episodes were asymptomatic. The ratio of asymptomatic to symptomatic AF episodes increased after ablation from 1.1 to 3.7 ($P=.002$). By symptoms alone, 29 of 50 patients (58%) were free of AF/AFL/AT after ablation compared with 23 of 50 (46%) using ICM-detected AF/AFL/AT recurrence. Asymptomatic episodes were more likely AFL/AT and were significantly shorter and slower, with lower heart rate variability. However, the postablation state was the strongest independent predictor of asymptomatic AF.

Conclusions: The ratio of asymptomatic to symptomatic AF episodes increased from 1.1 before to 3.7 after ablation. Postablation state is the strongest predictor of asymptomatic AF. Symptoms alone underestimate postablation AF burden, with 12% of patients having asymptomatic recurrences only.

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ATRIAL FIBRILLATION (AF) IS responsible for substantial morbidity, including disabling symptoms and stroke. Even brief asymptomatic AF episodes can substantially raise the risk for stroke.[1] Rhythm control does not necessarily reduce this risk, with 1 trial suggesting increased thromboembolic risk in patients receiving antiarrhythmics.[2] This increase likely resulted from withdrawal of anticoagulation therapy when antiarrhythmics appeared to control AF, yet asymptomatic AF persisted. Understanding asymptomatic AF is thus critically important.

Catheter ablation of AF has emerged as an effective treatment for this arrhythmia, with reported cure rates of 60% to 70% for paroxysmal AF after 1 or more procedures.[3] The term *cure*, however, is controversial because most studies determine recurrence rates based on patient symptoms. The incidence of asymptomatic AF is not well described before or after catheter ablation. Current data consist of single-center experiences, none of which have used continuous AF monitoring with an implantable cardiac monitor (ICM). Implantable cardiac monitors with automated AF detection have a very high sensitivity and specificity for the detection of AF.[4] Knowledge of the incidence of asymp-

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Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria
Age >18 y
First-time ablation procedure for AF
Symptomatic AF refractory to ≥1 antiarrhythmic; symptomatic patients should feel aware of AF as it occurs; symptoms may include palpitations, shortness of breath, chest pain, fatigue, other, or any combination
Paroxysmal or persistent AF; paroxysmal AF should include ≥4 episodes of AF in the 6 mo before assessment/ablation and is defined as AF that spontaneously terminates within 7 d; persistent AF is sustained for >7 d or lasts <7 d and requires pharmacologic or electrical cardioversion
≥1 Episode of AF must have been documented by ECG or Holter monitoring within 12 mo of inclusion in the study
No contraindication to systemic anticoagulation therapy with heparin sodium or warfarin sodium
Able and willing to provide written informed consent to participate
Exclusion Criteria
Permanent AF, defined as chronic, persisting AF (typically >1 y) for which cardioversion (pharmacologic or electrical) has failed or will never be attempted
AF believed to be secondary to an obvious reversible cause
Contraindications to systemic anticoagulation therapy with heparin or warfarin
Previous AF ablation
Pregnancy or possible pregnancy
Left atrial size ≥55 mm

Abbreviations: AF, atrial fibrillation; ECG, electrocardiography.

tomatic AF is important for accurate reporting of procedural success rates.

Finally, guidelines state that the primary indication for AF ablation is to reduce symptomatic AF and improve quality of life.[5,6] However, remarkably little is known about the mechanisms by which AF symptoms are perceived.[7] Features of a given AF episode that might or might not result in symptoms are not well understood[8]; continuous monitoring may enhance this understanding.

The purpose of this study was to use long-term continuous AF monitoring with an ICM to assess the incidence and predictors of symptomatic vs asymptomatic AF in symptomatic patients undergoing catheter ablation of AF.

METHODS

STUDY DESIGN

We conducted a multicenter prospective cohort study. The DISCERN AF trial (Discerning Symptomatic and Asymptomatic Episodes Pre and Post Radiofrequency Ablation of Atrial Fibrillation) was registered, and enrollment occurred from October 22, 2008, to August 28, 2009. Enrollment occurred at the following 8 centers: Southlake Regional Health Centre (n=14), Institut Universitaire de Cardiologie et Pneumologie de Québec (n=9), Queen Elizabeth II Hospital (n=7), McGill University Health Centre (n=6), Royal Jubilee Hospital (n=5), University of Ottawa Heart Institute (n=4), London Health Sciences Centre (n=4), and Hamilton Health Sciences Centre (n=1). All AF ablation specialists were experienced (>100 AF ablations/y per center). Patients but not investigators were blinded to ICM data. Data were managed by a central, independent study coordination center (University of Ottawa Heart Institute) with a restricted-access database. Written informed consent was obtained before patient inclusion. The study was approved by the ethics review board at each institution.

PATIENT POPULATION

Detailed inclusion and exclusion criteria are outlined in **Table 1**. Definitions of paroxysmal and persistent AF conform to the guidelines of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology.[6]

ICM IMPLANTATION AND ADJUDICATION

All patients underwent implantation of an ICM with an automatic AF detection algorithm that does not require patient activation (Reveal XT, Medtronic). The algorithm[4] is based on R-wave detection and analysis of the irregularity of the R-R intervals to define AF. This algorithm has an overall accuracy for AF detection of 98.5%.[4] The device was implanted at least 3 months before AF ablation and remained for a minimum of 18 months after ablation. The implantation and programming technique for the ICM was standardized across centers (described in the eMethods; http://www.jamainternalmed.com).

The ICM data were downloaded at each visit to reduce the probability of memory overflow. Even if memory capacity is exceeded, the device continues to collect total AF burden and episode data (without electrocardiograms [ECGs]). Every ICM event/ECG was adjudicated by 2 independent, blinded investigators (A.V. and D.B.). Episodes were classified as AF, atrial flutter (AFL), atrial tachycardia (AT), sinus, or artifact. Both investigators had to agree independently on the interpretation. In case of disagreement, the event was adjudicated by a third blinded investigator (J.S.). Committee review was planned if disagreement persisted (not required).

PATIENT SYMPTOM DIARY

Patients recorded their symptoms in a standardized diary (eFigure 1). The diary allowed for specification of the time, date, and duration of episodes. Specific, standardized instructions were provided on how to fill out the diary; the importance of entering precise times of symptom onset and offset was repeated at each study visit. Diaries were returned and new ones were issued at each study visit to minimize the loss of diary data.

CATHETER ABLATION PROCEDURE

The catheter ablation procedure has been reported previously[9] and is detailed in the eMethods. Circumferential radiofrequency lesions were placed around the pulmonary veins in the left atrium to isolate the pulmonary vein triggers for AF electrically. Repeated procedures were recommended for patients with ongoing recurrences beyond the first 3 months but within 6 months of the initial ablation.

FOLLOW-UP

Patients were followed up at 3, 6, 9, 12, 15, and 18 months after ablation, with ECG and 48-hour Holter monitoring at the 3-, 6-, 9-, and 12-month visits. The ICM data and symptom diaries were collected at each visit.

STUDY END POINTS

Because the ICM analyzes rhythm in increments of 2 minutes, a recurrence was defined as any episode of AF/AFL/AT of 2 minutes or longer. A symptomatic recurrence was defined as an ICM episode of atrial arrhythmia for which correlating symptoms were documented in the patient diary within 30 minutes before or after the start or the end of the ICM episode. All other

adjudicated episodes of arrhythmia were considered asymptomatic. The numbers of symptomatic vs asymptomatic days for each patient were calculated using previously published criteria[10]; any day with AF/AFL/AT lasting 5 minutes or longer detected by the ICM and with diary symptoms lasting 5 minutes or longer was considered symptomatic. If the detected AF/AFL/AT lasted at least 5 minutes but the diary symptoms lasted less than 5 minutes, the day was considered asymptomatic.

Procedural success was defined as the lack of any symptomatic or asymptomatic AF/AFL/AT of 2 minutes or more during the 3 to 18 months after the initial procedure, with or without the use of antiarrhythmics. The first 3 months were treated as a blanking period to allow healing as per the consensus guidelines of the Heart Rhythm Society.[11]

Secondary analyses consisted of (1) comparison of the procedural success rate as determined by ICM vs traditional symptom-based and intermittent Holter monitoring and (2) examination of the predictors of asymptomatic AF, including episode heart rate, episode duration, daily heart rate variability (HRV), type of arrhythmia recurrence, and interepisode time (defined as the time between 2 consecutive episodes of AF/AFL/AT), all of which are provided by the ICM. Heart rate variability is calculated by measuring 5-minute medians of the ventricular interval in milliseconds during sinus rhythm and calculating the standard deviation of those medians during 24 hours; this value constitutes a known indicator of parasympathetic activity (SDANN).[12]

SAMPLE SIZE AND STATISTICAL ANALYSIS

At the time that this protocol was designed, very few data were available to predict the incidence of asymptomatic AF in patients with symptomatic AF. Based on the sparse retrospective data published at the time, we estimated a cohort size of 50 patients targeting more than 1500 AF episodes for analysis. This sample size conservatively estimated 1 to 2 episodes of AF per month per patient for the 21 months of ICM use.

All data are reported as mean (SD) for continuous variables and frequencies with percentages for categorical variables unless otherwise indicated. To examine the predictors of asymptomatic AF/AFL/AT, we used the binary linear mixed-effects model for univariable and multivariable analysis to account for the correlations between repeated measures on the same patients over time. Odds ratios (95% CI) were reported. For the patient-level characteristics analysis, we used a multivariable linear regression model with the percentage of asymptomatic AF/AFL/AT as the dependent variable. A P value of less than .05 was considered significant for all statistical determinations. The analysis was performed using commercially available software (SAS, version 9.2; SAS Institute Inc).

RESULTS

PATIENT CHARACTERISTICS

Fifty patients were initially enrolled, but 1 patient did not undergo catheter ablation because of persistent left atrium thrombus. One additional patient was enrolled to meet the target of 50 patients. Patient characteristics are detailed in **Table 2**.

All patients underwent ICM implantation and catheter ablation and completed all follow-up visits. Diary adherence was excellent, with 100% of patients returning diaries at each follow-up and 86.9% of diaries containing at least 1 entry. In total, 5013 diary entries were made by 50 patients, exceeding the number of ICM AF episodes and symptomatic AF days.

Table 2. Baseline Patient Characteristics[a]

Characteristic	Data
Age, mean (SD), y	57 (11)
Male sex	32 (64)
Paroxysmal AF	40 (80)
Persistent AF	10 (20)
Canadian Cardiovascular Society Severity of AF Score, mean (SD)	3 (1)
No. of failed antiarrhythmics administered before ablation, mean (SD)	1.2 (0.7)
Duration of AF symptoms before ablation, median (range), y	6.2 (1-32)
CHADS index, mean (SD)	1.4 (0.3)
Hypertension	15 (30)
Diabetes mellitus	5 (10)
Sleep apnea	5 (10)
Prior stroke/TIA	4 (8)
Coronary artery disease	3 (6)
Heart failure	3 (6)
Valvular heart disease	2 (4)
Ejection fraction, mean (SD)	54 (10)
Left atrial diameter, mean (SD), mm	41 (6)

Abbreviations: AF, atrial fibrillation; CHADS, index that quantifies stroke risk by congestive heart failure, hypertension, age greater than 75 years, diabetic, and history of stroke; TIA, transient ischemic attack.
[a] Unless otherwise indicated, data are expressed as number (percentage) of patients (n = 50).

Table 3. Classification of Arrhythmia by Episode and Cumulative Duration of the Episodes

	Proportion of Episodes, %[a]	Proportion of Total Duration, %
AF	54.0	98.0
AFL/AT	15.0	1.5
Sinus with extrasystoles	16.0	0.3
Sinus arrhythmia	4.0	0.2
Artifact	11.0	0.1

Abbreviations: AF, atrial fibrillation; AFL/AT, atrial flutter/atrial tachycardia.
[a] Indicates proportion of 2355 episodes.

ICM EPISODE ADJUDICATION

In total, the ICMs of all patients cumulatively logged 1 933 100 minutes of arrhythmia, of which 1 086 572 minutes (56.2%) was stored as 2355 discrete episodes with accompanying ECGs for adjudication. Classification of the arrhythmia by episode and by cumulative duration of the episodes is shown in **Table 3**. By number of episodes, 69.0% represented AF/AFL/AT. When measured by duration, 99.5% of the stored episode duration represented AF/AFL/AT. The median duration of artifact recordings was 2 (range, 2-5) minutes.

AF/AFL/AT BURDEN BEFORE AND AFTER ABLATION

Before ablation, the mean AF/AFL/AT burden was 2.0 h/d per patient. Catheter ablation achieved a reduction in AF/AFL/AT burden by 86% to 0.3 h/d per patient ($P < .001$). The total number of days per month with more than 5

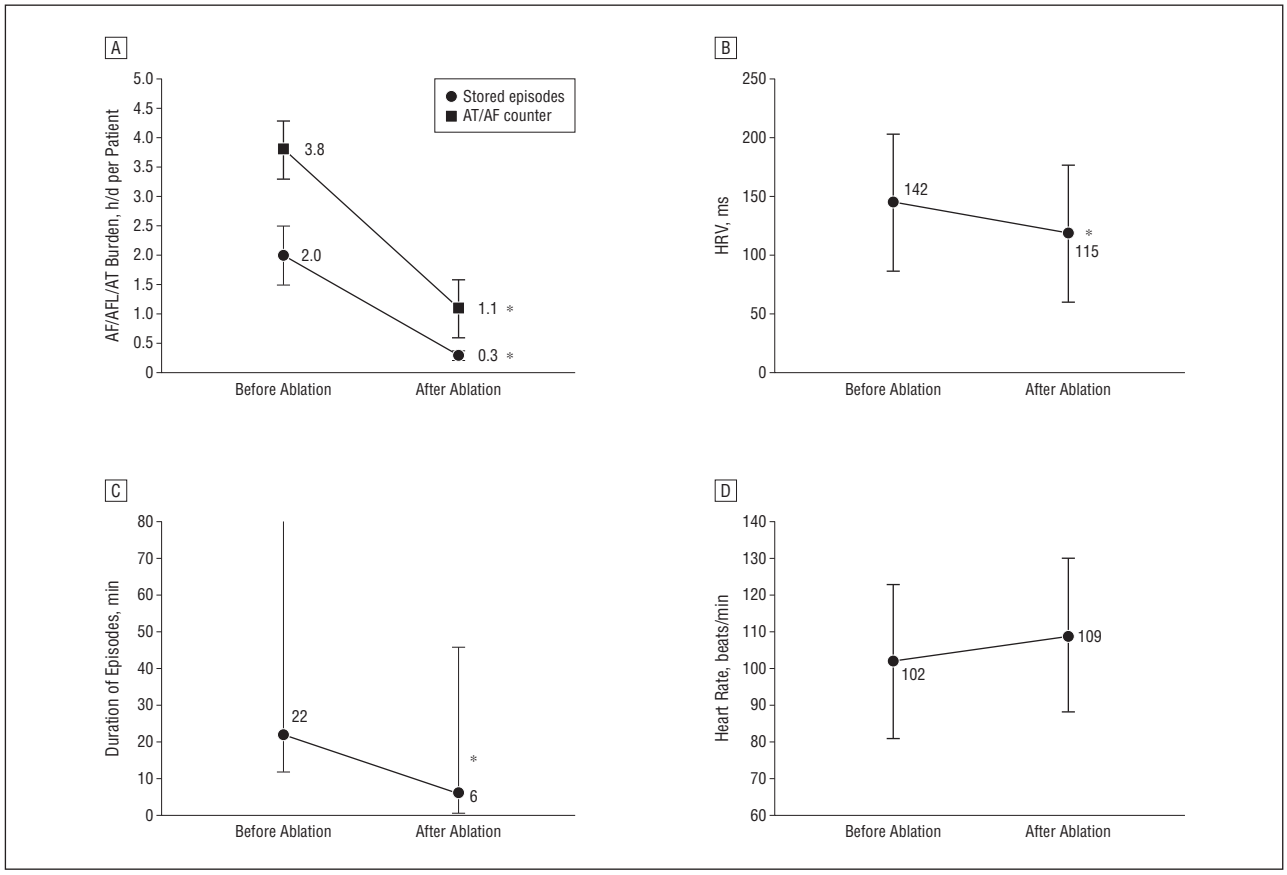

Figure 1. Data obtained from implantable cardiac monitors showing changes after catheter ablation. A, Before ablation, the mean atrial fibrillation/atrial flutter/atrial tachycardia (AF/AFL/AT) burden was 2.0 h/d per patient. Catheter ablation achieved a substantial reduction in AF/AFL/AT burden whether measured by the duration of stored episodes with electrocardiographic recordings or by the continuous AT/AF counter ($P \leq .001$). B, Heart rate variability (HRV) significantly decreased after ablation from a mean (SD) of 142 (61) to 115 (57) milliseconds ($P = .002$). C, Duration of episodes after ablation were shorter, decreasing to a median of 6 (interquartile range, 5-40) from 22 (10-202) minutes ($P < .001$). D, Heart rate did not change significantly. *$P < .05$ compared with preablation values.

Table 4. Predictive Accuracy for ICM-Detected Episodes of AF/AFL/AT

	Predictive Value, %	
	Positive	Negative
Patient symptoms	86.9	23.6
Intermittent ECG (every 3 mo)	33.3	94.9
Intermittent 48-h Holter monitoring (every 3 mo)	0	94.4

Abbreviations: AF/AFL/AT, atrial fibrillation/atrial flutter/atrial tachycardia; ECG, electrocardiography; ICM, implantable cardiac monitor.

minutes of AF/AFL/AT dropped from 13.0 to 5.0 per patient ($P = .001$), and the number of symptomatic days per month dropped from 4.3 to 0.6 per patient ($P = .002$). Postablation episodes were significantly shorter, decreasing to a median of 6 (interquartile range, 5-40) from 22 (10-202) minutes ($P < .001$). Heart rate variability also decreased after ablation from 142 (61) to 115 (57) milliseconds ($P = .002$). Changes in arrhythmia burden and characteristics are depicted in **Figure 1**.

ABLATION SUCCESS RATE BY SYMPTOMS, HOLTER/ECG, AND ICM

The mean number of procedures was 1.4 (0.6) per patient, and the mean time from the first to the second ablation procedures was 6 (2) months. At final follow-up, 3 of 50 patients (6%) continued to receive antiarrhythmic therapy (flecainide acetate for 2 and sotalol hydrochloride for 1).

When success was defined on the basis of symptoms alone, 29 of 50 patients (58%) were free of arrhythmia after all ablations. If recurrence was defined as symptoms or as detection of a recurrence by ECG or 48-hour Holter monitoring, then freedom from atrial arrhythmia was seen in 28 patients (56%). If recurrence was defined as any AF/AFL/AT detected on ICM, the success rate fell to 46% (23 patients) (eFigure 2), indicating that 6 patients (12%) had exclusively asymptomatic episodes of recurrent arrhythmia.

Positive and negative predictive values for patient symptoms and intermittent use of ECG and Holter monitoring for ICM-detected episodes of AF/AFL/AT are detailed in **Table 4**.

ASYMPTOMATIC AF/AFL/AT BEFORE AND AFTER ABLATION

Before and after ablation, a greater proportion of AF/AFL/AT duration was asymptomatic. In total, 69.0% of all episodes, or 56.0% of the total AF/AFL/AT duration, did not have any associated diary entry and

were considered asymptomatic. A total of 7316 days had more than 5 minutes of AF/AFL/AT, of which 71.0% were asymptomatic. One hundred sixty days (2.2%) had documented diary symptoms but no detection of arrhythmia by the ICM.

The proportion of episodes that were asymptomatic increased from 52.0% before to 79.0% after ablation ($P = .002$; **Figure 2**). The ratio of asymptomatic to symptomatic AF episodes increased from 1.1 before to 3.7 after ablation. The proportion of asymptomatic AF/AFL/AT duration increased from 36.0% before to 68.0% after ablation ($P < .001$). The number of arrhythmia days that were asymptomatic also increased a similar amount from 58.0% before ablation to 77.0% after ablation ($P = .003$). Most patients with asymptomatic arrhythmia episodes after ablation also had symptomatic episodes (6 [12%] had exclusively asymptomatic episodes after ablation).

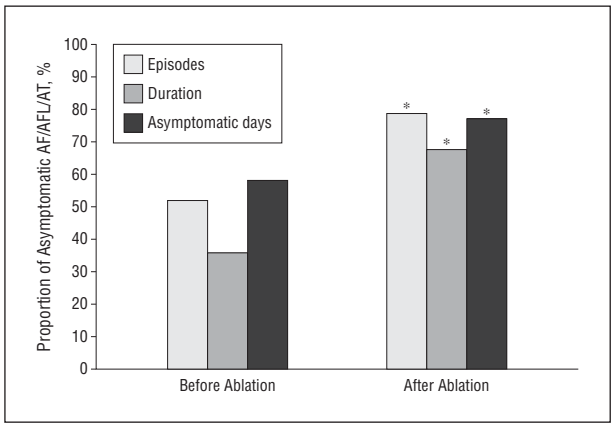

Figure 2. The percentage of asymptomatic atrial fibrillation/atrial flutter/atrial tachycardia (AF/AFL/AT) in patients before and after ablation. Whether measured by the percentage of AF/AFL/AT episodes, the total duration of the episodes, or the percentage of asymptomatic days, the percentage of asymptomatic AF/AFL/AT significantly increases after ablation ($P < .005$ for all). *$P < .05$ compared with preablation values.

PREDICTORS OF ASYMPTOMATIC AF/AFL/AT

Arrhythmia events after ablation were 3 times more likely to be asymptomatic compared with preablation episodes, and the postablation state was the strongest predictor of asymptomatic AF/AFL/AT by univariable analysis (odds ratio, 3.19 [95% CI, 2.53-4.01]; $P < .001$) (**Table 5**). The number of AFL/AT episodes ($P < .001$) and the number of episodes without antiarrhythmics/β-blockers ($P < .001$), with lower HRV ($P < .001$), and with a lower heart rate ($P = .003$) were also more likely to be asymptomatic (Table 5). The number of patients using specific medications before and after ablation is detailed in the eTable. We found a trend toward a shorter duration predicting asymptomatic episodes ($P = .05$), and interepisode time did not have any significant impact (Table 5). Although procedural success varied from site to site, the success rates of individual sites were not significant predictors of asymptomatic AF/AFL/AT (odds ratio, 1.18 [95% CI, 0.90-1.55]; $P = .21$) (eFigure 3).

By multivariable analysis, the postablation state remained the strongest independent predictor of asymptomatic AF/AFL/AT (**Table 6**). Episodes of AFL/AT, lower HRV, lower heart rate, and shorter episode duration were also significant (Table 6). No patient characteristics were significant predictors of asymptomatic AF/AFL/AT, specifically age ($\beta = 0.61$; $P = .27$), female sex ($\beta = -2.12$; $P = .87$), paroxysmal vs persistent AF ($\beta = -3.45$; $P = .78$), the presence of hypertension ($\beta = -3.23$; $P = .78$), duration of AF history ($\beta = -0.10$; $P = .14$), and left atrium size ($\beta = 0.03$; $P = .98$).

COMMENT

To our knowledge, this study is the first prospective multicenter study to examine the incidence and predictors of asymptomatic AF after ablation using continuous ICM monitoring. Although ablation significantly reduces the burden of AF, the proportion of asymptomatic AF episodes increases. Asymptomatic episodes were more likely to be AFL/AT, were slower and shorter, and had lower HRV. The use of antiarrhythmics and the rate of individual site success did not predict asymptomatic AF independently. However, the postablation state was the strongest independent predictor of asymptomatic AF/AFL/AT. Consequently, procedural success is overestimated by patient symptoms, even when combined with intermittent Holter monitoring, with 12% of patients having exclusively asymptomatic recurrence. Our findings suggest that caution should be exercised before stopping oral anticoagulation therapy after ablation and emphasize the need for ongoing continuous monitoring.

Long-term continuous monitoring of AF should be able to detect more AF compared with symptom reporting or intermittent monitoring.[10] However, the few single-center studies examining asymptomatic AF after ablation show mixed results based mostly on intermittent monitoring. Three studies demonstrated an excellent correlation between symptoms and AF detected by transtelephonic monitoring or a permanent pacemaker,[13-15] but they were limited by short follow-up and the limited ability of older algorithms on pacemakers to detect AF. In contrast, other studies have shown incidences of asymptomatic AF ranging from 5% to 44% of patients,[16-19] but only 1 study used continuous ICM monitoring.[20] Unfortunately, that study did not report patient success rate or the incidence of exclusively asymptomatic recurrences.

Our study is the only multicenter, prospective, long-term study to assess asymptomatic AF recurrence after ablation using continuous monitoring. Symptoms, intermittent Holter monitoring, and ECGs had poor predictive accuracy for AF episodes detected by the ICM. Despite 10 000 hours of external monitoring, only 1 additional patient failure was detected compared with symptoms alone. In contrast, ICM detected 12% of patients with purely asymptomatic AF. Two prior single-center studies demonstrated even higher rates of purely asymptomatic AF (37%-44%),[16,17] but they used only intermittent monitoring and were performed when definitive demonstration of pulmonary vein isolation was not a prerequisite for ablation. The lack of complete isolation may have increased the incidence of asymptomatic arrhythmia.

We do not know why symptoms of AF vary tremendously between patients. This study is the first to sys-

Table 5. Characteristics of Asymptomatic vs Symptomatic Episodes of AF/AFL/AT

Characteristic	Asymptomatic Episode	Symptomatic Episode	OR (95% CI)	*P* Value
Ratio of postablation to preablation state	3.0	0.9	3.19 (2.53-4.01)	<.001
Ratio of AF to AFL/AT	3.2	6.6	2.03 (1.49-2.76)	<.001
Ratio of no drug to AAD	0.4	0.2	1.69 (1.28-2.23)	<.001
HRV, mean (SD), ms	116 (57)	142 (62)	1.07 (1.05-1.09)[a]	<.001
Heart rate, mean (SD), beats/min	105 (22)	110 (22)	1.08 (1.03-1.14)[a]	.003
Episode duration, median (IQR), min	4 (2-26)	16 (4-138)	1.00 (1.00-1.00)[a]	.05
Interepisode time, median (IQR), h	96 (18-2234)	62 (10-2744)	1.00 (1.00-1.00)	.3

Abbreviations: AAD, any antiarrhythmic, including β-blockers; AF/AFL/AT, atrial fibrillation/atrial flutter/atrial tachycardia; HRV, heart rate variability; IQR, interquartile range; OR, odds ratio.
[a] Odds ratio was calculated for 10 units lower for HRV, heart rate, and episode duration.

Table 6. Multivariable Analysis for Predictors of Asymptomatic Episodes of AF/AFL/AT

Variable	OR (95% CI)	*P* Value
After vs before ablation	2.66 (1.97-3.59)	<.001
AFL/AT vs AF	1.88 (1.34-2.65)	<.001
Lower heart rate (per 10 beats/min)	1.16 (1.09-1.24)	<.001
Lower HRV (per 10 ms)	1.05 (1.03-1.08)	<.001
Shorter episode duration (per 10 min)	1.01 (1.00-1.01)	.004
No drug vs any AAD	1.36 (0.96-1.92)	.08
Interepisode time, h	1.00 (1.00-1.00)	.3

Abbreviations: AAD, any antiarrhythmic, including β-blockers; AF/AFL/AT, atrial fibrillation/atrial flutter/atrial tachycardia; HRV, heart rate variability; OR, odds ratio.

tematically examine the effect of AF episode characteristics on symptoms. The postablation state was the strongest predictor of asymptomatic AF. One explanation may be a change in autonomic innervation after ablation. Reduced HRV is an indicator of lower vagal tone, and lower HRV was also a predictor of fewer symptoms. However, the postablation state remained an independent predictor of asymptomatic AF even after correcting for HRV, suggesting changes that might not be detected by HRV alone. One also cannot rule out the possibility of a placebo effect after ablation, and recent studies have reported that improvement in quality of life may be independent of procedural success.[21,22] However, overall arrhythmia burden was substantially reduced by ablation in this study.

This study is, to our knowledge, the first to show that episode duration affects symptoms, with asymptomatic AF episodes being significantly shorter. Slower heart rate also predicted asymptomatic episodes. Heart rate control has always been assumed to affect AF symptoms and quality of life, but prior studies have shown mixed results.[23-25] None of those studies had the ability to assess the effect of heart rate on individual episodes of arrhythmia. In addition, AF was more likely to be symptomatic compared with AFL/AT. Perhaps the irregularity of rhythm during AF makes it more likely to be perceived, but this contrasts with anecdotal evidence that postablation AFL is typically symptomatic. With so few AFL/AT episodes in our preablation data set, no definitive conclusions can be made.

Procedural success rate and the use of antiarrhythmics have also been suggested as important contributors to patient symptoms.[17] Inadequate ablation may create asymptomatic recurrence. Antiarrhythmics or β-blockers may also blunt patient perception of arrhythmia. Site-specific success rates and the presence of drugs were not found to predict symptoms independently in this study.

Previous studies have shown that patient factors associated with more symptoms include female sex,[26] paroxysmal AF,[27] younger age,[28] and negative emotions.[26,29] We did not find any patient-level variable to be predictive of symptoms, but our study was underpowered to examine this question.

Our study has limitations. The definition of asymptomatic arrhythmia episodes was based on patient diary entries, and we cannot ensure that patients were 100% adherent in completing their diaries. However, 87% of diaries contained at least 1 entry at each follow-up, and the total number of diary entries exceeded the numbers of ICM AF episodes and symptomatic AF days. We found no significant decline in diary entries over time (9-18 months after ablation). The ICM had only the AF detection algorithm turned on, whereas when the AT detection was turned off; AT episodes may have been missed. However, prior data have shown that more than 55% of ATs have enough irregularity to be detected by the AF algorithm.[30] The AT detection algorithm results in a very high false-positive rate of sinus tachycardia detection, which would have substantially overestimated AF/AFL/AT burden and likely the proportion of asymptomatic atrial arrhythmia in our study.

In conclusion, the ratio of asymptomatic to symptomatic AF episodes increased from 1.1 before to 3.7 after ablation. The strongest predictor of asymptomatic AF was the postablation state. Symptoms alone underestimate AF burden after ablation, with 12% of patients having asymptomatic recurrences only.

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Online-Only Material: The eMethods, eFigures, and eTable are available at http://www.jamainternalmed.com.

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INVITED COMMENTARY

Atrial Fibrillation Ablation, Symptoms, and Stroke Risk

The public health burden of atrial fibrillation (AF) is considerable: AF affects an estimated 2.6 million Americans[1] and increases the risk for ischemic stroke 2- to 7-fold, likely as a result of thromboemboli from the left atrium. Most patients require treatment with anticoagulants to reduce the risk for stroke, but these therapies increase the risk for bleeding. Many but not all patients with AF experience arrhythmia-related symptoms such as palpitations, syncope, and reduced-exercise capacity. Thus, the therapy for AF aims to reduce arrhythmia-related symptoms and the risk for ischemic stroke.

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One strategy to manage AF is to restore and maintain sinus rhythm. The outcomes of using drugs for rhythm control have been largely disappointing. In the landmark Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial,[2] patients randomized to rhythm control or to ventricular rate control had similar rates of all-cause mortality. Patients in the rhythm control treatment arm exhibited a trend toward increased ischemic stroke, driven largely by ischemic strokes that occurred after discontinuation of anticoagulation therapy. This observation suggests that patients with a history of AF should continue anticoagulation therapy indefinitely based on their underlying stroke risk profile, a position that is maintained in current guidelines.[3]

Atrial fibrillation ablation is a newer approach to rhythm control, in which radiofrequency energy or cryotherapy is used to isolate the pulmonary veins and ablate arrhythmogenic foci. The efficacy and safety of this procedure continues to improve, based on techniques, such as intravascular ultrasonographic guidance of the transseptal puncture and electroanatomic mapping to guide the ablation. Nevertheless, procedural complications are not uncommon,[4] many patients have recurrent AF, and AF ablation is expensive (average cost, $15 000-$20 000 in the Medicare population).

Atrial fibrillation ablation may still provide clinical value by mitigating arrhythmia-related symptoms and, possibly, by reducing the risk for stroke. In this issue of the journal, Verma and colleagues[5] provide key insights into how AF ablation addresses these therapeutic goals.

The investigators in this multicenter study used small, subcutaneous, implanted cardiac monitors to evaluate the recurrence of AF after catheter ablation. They prospectively enrolled 50 patients with symptomatic AF (40 with paroxysmal and 10 with persistent AF) who underwent pulmonary venous isolation at experienced centers (>100 procedures per year). Patients had a monitor implanted at least 3 months before their first AF ablation and were observed for at least 18 months afterward. Patients had been symptomatic for a median of 6.2 years before the procedure and had relatively low risk for stroke (mean score of 1.4, based on 1 point each for congestive heart failure, hypertension, age >75 years, and diabetes, and 2 points for a history of stroke), suggesting an annual rate of stroke of 2.8 to 4.0 per 100 patient-years.[6] The investigators correlated patient symptom diaries with data periodically downloaded from the implanted monitors to establish the frequency of recurrence of symptomatic and asymptomatic AF.

The study provides some important insights, despite its small sample size. In aggregate, AF ablation decreased the atrial arrhythmia burden by 86%, from 2.0 to 0.3 hours per patient per day ($P<.001$). Episodes of AF after ablation were shorter (from a median of 22 to 6 minutes; $P<.001$), less irregular, and more likely to be asymptomatic (from 52% before to 79% after ablation; $P=.002$). The success rate of AF ablation depended on how recurrences were measured. Fifty-eight percent of the patients had no episodes of symptomatic AF, but only 46% of the patients had a successful procedure based on the elimination of symptomatic and asymptomatic recurrences at 18 months. Six patients (12%) in this small study had exclusively asymptomatic recurrences that would not have been detected without an implantable monitor.

These results have 2 key implications. First, in this contemporary series of AF ablations performed at experienced centers, a little more than half of the patients were symptom free at 18 months, despite a mean of 1.4 ablations. This relatively high rate of recurrent AF is disappointing and suggests that AF is difficult to eliminate even with highly aggressive therapy.

Second, because AF episodes increase the risk for stroke whether they cause symptoms or not, even patients who are asymptomatic after AF ablation remain at increased risk for stroke. Although the reduction of symptoms is cer-