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Time Course for Resolution of Left Atrial Appendage Stunning After Catheter Ablation of Chronic Atrial Flutter

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OBJECTIVES This study assessed the time course of resolution of left atrial appendage (LAA) stunning after catheter ablation of chronic atrial flutter (AFL).

BACKGROUND Although the presence of LAA stunning after ablation of chronic AFL calls for anticoagulation in the post-cardioversion period, limited information has been obtained, particularly regarding its duration.

METHODS Sixteen patients who underwent ablation of chronic, pure AFL were studied, only five of whom had structural heart disease and one of whom had a reduced left ventricular ejection fraction. The LAA emptying velocities (LAAEV) and left atrial spontaneous echo contrast (SEC) were assessed using transesophageal echocardiography before, within 24 h after, one week after, and two weeks after ablation.

RESULTS Within 24 h after ablation, the LAAEV decreased from 39 ± 10 cm/s during AFL to 21 ± 10 cm/s during sinus rhythm ($p < 0.01$), with eight patients (50%) having documented SEC. After one week, the LAAEV increased (39 ± 17 cm/s, $p < 0.01$ vs. within 24 h) and SEC resolved in five of eight patients. After two weeks, the increase in LAAEV persisted (54 ± 14 cm/s, $p < 0.01$ vs. 1 week) and SEC was no longer present in any of the patients. The numbers of patients with LAAEV >30 cm/s and absence of SEC were three within 24 h, 11 at one week, and 16 at two weeks after ablation.

CONCLUSIONS Patients with chronic, pure AFL and preserved left ventricular function who will undergo catheter ablation may not require anticoagulation therapy for more than two weeks after the procedure because of the presence of forceful mechanical LAA contractions and the absence of SEC. (J Am Coll Cardiol 2003;41:2207–11) © 2003 by the American College of Cardiology Foundation

Although anticoagulation at the time of cardioversion should be considered for patients with atrial flutter (AFL) in the same manner as anticoagulation for patients with atrial fibrillation (AF) (1), whether anticoagulation is necessary after AFL cardioversion is still a controversial issue in the light of the absence of any controlled trial on the efficacy of anticoagulation in the post-cardioversion period of AFL (2). There is a solid reason, however, to consider anticoagulation in the post-cardioversion period for patients with AFL. Transient left atrial appendage (LAA) dysfunction after electrical cardioversion of AF and AFL is known to occur (i.e., LAA stunning) and is thought to be commonly associated with thrombus formation and embolic stroke (3,4). Moreover, LAA stunning also occurs after chronic AFL cardioversion by catheter ablation (5,6).

At present, curative catheter ablation is fast becoming the initial therapy for chronic AFL, emphasizing the need for further information on LAA stunning and the duration of anticoagulation therapy after cardioversion of chronic AFL (2). So far, only one study has practically investigated the return of depressed LAA function to normal values after cardioversion in patients with AFL by using transesophageal echocardiographic (TEE) examinations and has provided information on the required duration of anticoagulation therapy in the post-cardioversion period (5). The study had the intervening period between the examinations (interval between 30 min and 3 weeks post-cardioversion), which prevented determination of the exact time course for recovery of LAA function.

The aims of the present study were to assess the time course of resolution of LAA stunning after AFL cardioversion by catheter ablation intimately and to gain insight into the required duration of anticoagulation therapy in the post-cardioversion period.

METHODS

Patient population. Nineteen consecutive patients with chronic, typical AFL lasting more than one month, without a history of AF (i.e., chronic, pure AFL), who were undergoing catheter ablation were recruited. The patients who did not maintain sinus rhythm (SR) before completion of serial TEE studies or could not complete scheduled TEE were excluded from the study. After giving written, informed consent, all study patients underwent TEE, electrophysiologic study, and catheter ablation. This study was approved by our institutional review board.

Definition of atrial flutter. Typical AFL was considered present if: 1) the surface electrocardiogram (ECG) demon-

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JACC Vol. 41, No. 12, 2003
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Abbreviations and Acronyms

AF	= atrial fibrillation
AFL	= atrial flutter
ECG	= electrocardiogram
LA	= left atrium/atrial
LAA	= left atrial appendage
LAAEV	= left atrial appendage emptying velocity
LVEF	= left ventricular ejection fraction
SEC	= spontaneous echo contrast
SR	= sinus rhythm
TEE	= transesophageal echocardiography

strated negative or positive flutter waves in the inferior limb leads and lead V_1, with a regular atrial rate; and 2) the electrophysiologic study confirmed that the flutter reentrant circuit involved a tricuspid valve annulus–inferior vena cava orifice/eustachian ridge isthmus, based on the activation and entrainment mapping technique (7). "Chronic AFL" was defined as AFL documented repeatedly on a surface ECG without evidence of intermittent SR at consecutive outpatient visits before study inclusion. The total arrhythmia duration was defined as the duration of the arrhythmia starting from the first episode of documented AFL.

Ablation procedure. After completion of the electrophysiologic study, anatomically guided linear ablation of the isthmus was performed with a 4-mm tip ablation catheter. Radiofrequency pulses were delivered with the temperature preset to 60°C for 60 s. A line of sequential overlapping lesions was created beginning at the tricuspid valve annulus, with stepwise withdrawal of the catheter until the last lesion was delivered at the inferior vena cava/eustachian ridge. The procedural end point was the termination of AFL and production of bi-directional conduction block through the isthmus.

Echocardiographic examination. To assess serial changes in LAA function, TEE was conducted the day before ablation, within 24 h after (19 ± 2 h [range 17 to 23]), one week after, and two weeks after restoration of SR (Fig. 1). Patients were mildly sedated, if necessary, with intravenous hydroxyzine hydrochloride before TEE probe intubation. Then, TEE was performed using a commercially available ultrasound system (SSA-380A, Toshiba Inc., Tokyo, Japan) equipped with a 5-MHz multiplane TEE probe.

After achieving adequate LAA imaging, the following measurements were made: LAA emptying flow velocities (LAAEV), spontaneous echo contrast (SEC), and thrombus in the left atrium (LA), including LAA. The peak LAAEV during a cardiac cycle was measured by pulsed Doppler echocardiography, positioning a sample volume at the level of the orifice. The measurement was obtained as an average of over five consecutive cardiac cycles. "Spontaneous echo contrast" was defined as the presence of dynamic intracavitary echoes with a characteristic swirling pattern distinct from white-noise artifact. The degree of SEC was graded as absent, mild, or severe (8,9). A thrombus was identified as an echo-dense intracavitary mass distinct from the underlying endocardium and not caused by pectinate muscle (10).

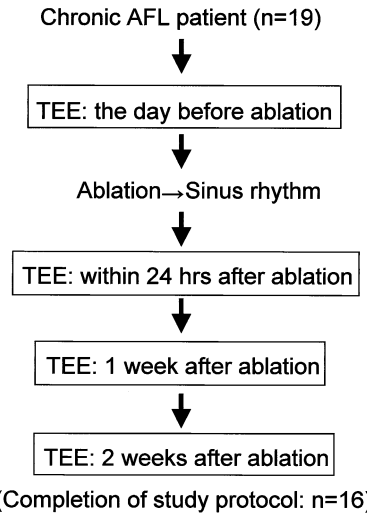

Figure 1. Flow diagram of transesophageal echocardiography (TEE) protocol. AFL = atrial flutter.

Transthoracic echocardiography was also performed the day before ablation to determine the LA, left ventricular end-diastolic, and end-systolic diameters. Left ventricular fractional shortening and left ventricular ejection fraction (LVEF) were derived from these measurements (11). One investigator who had no knowledge of the patients' clinical information analyzed all echocardiographic data.

Anticoagulation therapy. Before and after ablation, all patients received anticoagulation therapy with warfarin, targeting an international normalized ratio of 2.0 to 2.5. After restoration of SR, anticoagulation was discontinued when LAAEV >30 cm/s and the absence of SEC were both confirmed, except in the case of demonstrable LA or LAA thrombus.

Statistical analysis. Data are presented as the mean value ± SD and range or frequencies. The intergroup differences for continuous echocardiographic variables were evaluated by repeated measures of analysis of variance, applying the post hoc Scheffé test. A value of $p < 0.05$ was considered statistically significant. Analyses were performed with SAS statistical software (Stat View, version 5.0).

RESULTS

Patient characteristics. Although all patients were restored to SR immediately after ablation, three were excluded from the data analysis because of the development of AF, pacemaker implantation due to recurrent symptomatic sinus arrest lasting >3.0 s, or an inability to consent to subsequent TEE after ablation. Therefore, data from 16 patients were included in the analysis. The clinical and echocardiographic characteristics of these patients are summarized in Table 1. Structural heart disease was present in five patients (31%), one of whom had a reduced LVEF <40%. Eight patients

Table 1. Clinical and Transthoracic Echocardiographic Characteristics in Study Patients (n = 16)

Age (yrs)	64 ± 7
Gender (male/female)	15/1
Flutter cycle length (ms)	233 ± 23
Arrhythmia duration (months; range)	25 ± 37 (2–134)
Underlying disease* (n)	
Coronary artery disease	3
Valvular heart disease	1
Congenital heart disease	1
Dilated cardiomyopathy	1
Systemic hypertension	5
Diabetes mellitus	4
Lone arrhythmia	8
Previous embolic history	0
Echocardiographic variables	
LAD (mm; range)	44 ± 6 (30–58)
LVEDD (mm; range)	48 ± 6 (40–65)
LVFS (%; range)	30 ± 8 (8–44)
LVEF (%; range)	59 ± 13 (18–74)

*More than one per patient possible.
LAD = left atrial diameter; LVEDD = left ventricular end-diastolic diameter; LVFS = left ventricular fractional shortenig; LVEF = left ventricular ejection fraction.

(50%) did not have structural heart disease, hypertension, or diabetes mellitus. No patient had a history of embolism.

Left atrial appendage function. A recent study demonstrated that LAA function after AFL ablation may be dependent on heart rate (12). In this study, there were no significant differences in the sinus rate of the patients at each TEE examination after ablation. Serial changes in LAAEV and an example of serial changes in LAA pulsed Doppler flow are shown in Figures 2 and 3, respectively. The LAAEV decreased from 39 ± 10 cm/s (range 21 to 56) during AFL to 21 ± 10 cm/s (range 8 to 40) during SR at the time of first TEE after ablation ($p < 0.01$). After one week, the LAAEV increased to 39 ± 17 cm/s (range 13 to 69; $p < 0.01$ vs. within 24 h). After two weeks, the LAAEV continued to increase to 54 ± 14 cm/s (range 31 to 86; $p <$ 0.01 vs. 1 week). Furthermore, the LAAEV at two weeks after restoration of SR was greater than that during AFL ($p < 0.01$). Stunning of the LAA, which was defined as a decrease in LAAEV from before to after cardioversion of at least 20% (3), was observed in 12 patients (75%) within 24 h, in 5 patients (31%) at one week, and in no patients at two weeks after ablation.

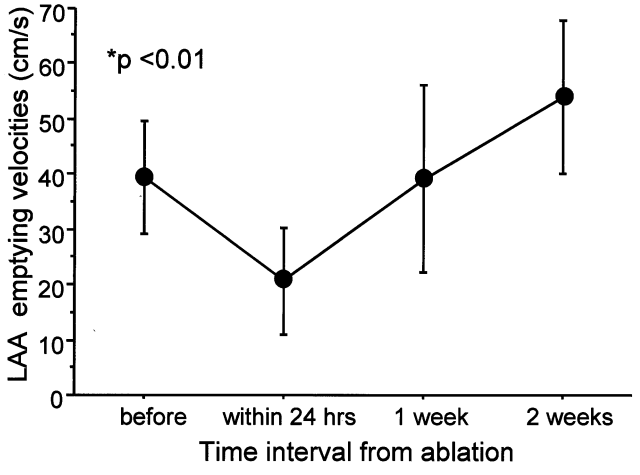

Figure 2. Serial changes in left atrial appendage (LAA) emptying flow velocities in patients with chronic atrial flutter before and after ablation. *By repeated measures of analysis of variance. **Vertical bars** indicate the mean value ± SD.

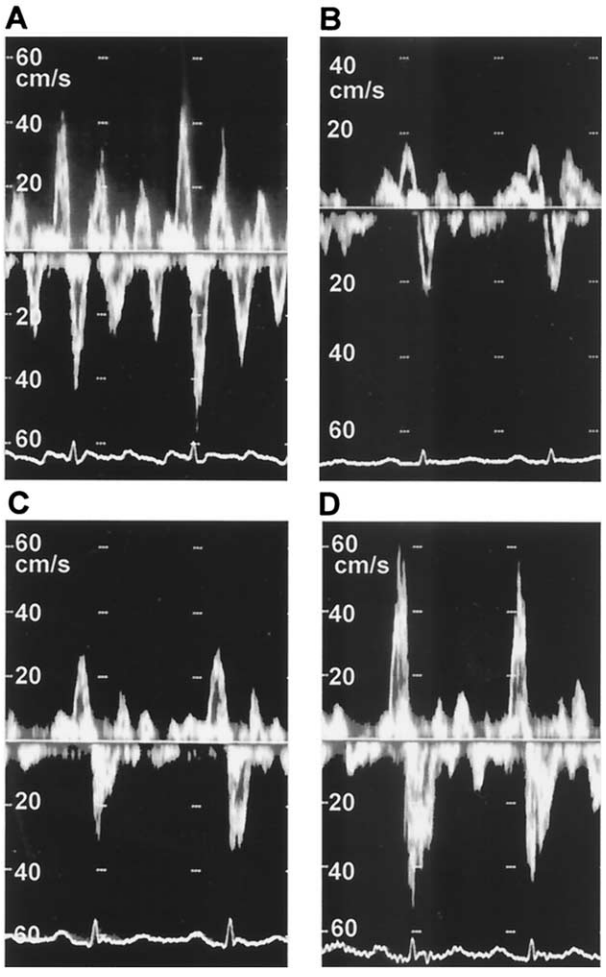

Figure 3. The left atrial appendage flow velocities are shown during atrial flutter **(A)** and sinus rhythm of 20 h **(B)**, 1 week after ablation **(C)**, and 2 weeks after ablation **(D)**. Paper speed of 50 mm/s.

Discontinuation of anticoagulation therapy. The TEE examination within 24 h after ablation demonstrated new or increased SEC in eight patients (Fig. 4). Two weeks after ablation, the SEC had disappeared and the LAAEV exceeded 30 cm/s in all of the patients (Table 2). The cumulative number of patients who had discontinuation of anticoagulation therapy was 3 (19%) within 24 h, 11 (69%) at one week, and 16 (100%) at two weeks after ablation. Neither LA nor LAA thrombus was detected in any of the patients by serial TEE examinations.

Atrial arrhythmia recurrence and thromboembolic events. During the follow-up period of at least six weeks, no patient had evidence of either AFL recurrence or AF, except for one patient who developed AF (mentioned in "Patient charac-

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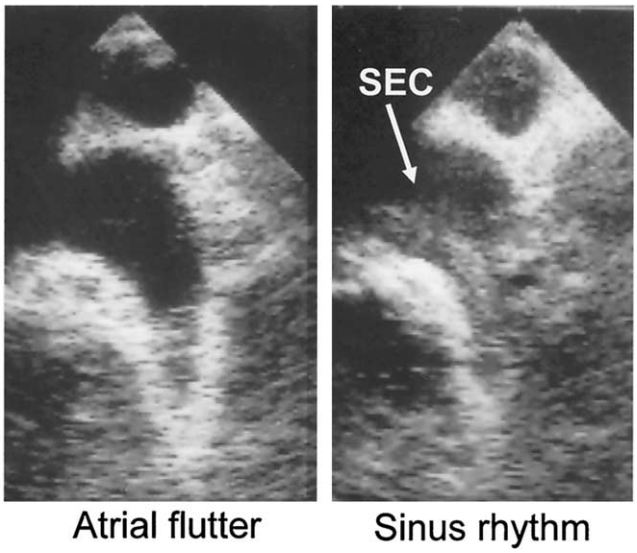

Figure 4. The spontaneous echo contrast (SEC) grade before and after atrial flutter ablation.

teristics"). Similarly, there were no thromboembolic events in any of the patients.

DISCUSSION

To avoid stroke subsequent to ablation of chronic AFL, anticoagulation therapy should be maintained even after the procedure, in the light of the presence of LAA stunning. This study demonstrates that within two weeks after catheter ablation of chronic, pure AFL, forceful mechanical LAA contractions are restored, and anticoagulation could thereby be discontinued safely if the patient remains in SR. These findings suggest that patients with chronic, pure AFL who undergo catheter ablation may not require anticoagulation therapy for more than two weeks after the procedure. We believe these findings provide important clinical information on anticoagulation therapy.

Anticoagulation and cardioversion. Significant LAA stunning could continue for at least 15 min (4), and LAA thrombus formation could be led by LAA stunning after AFL cardioversion (6). Recently, Gallagher et al. (13) demonstrated that the incidence of embolism after cardioversion of AFL is similar to that of cardioversion of AF and is appreciable (0.72% vs. 0.46%) when the duration of post-cardioversion anticoagulation is not strictly structured. Therefore, it may be adequate that anticoagulation is recommended for three to four weeks before and after cardioversion of patients with chronic AFL, as well as that of patients with chronic AF (1). Nevertheless, Grimm et al. (3) hypothesized that the duration of anticoagulation required after AFL cardioversion is likely to be significantly shorter than that required for AF, because the return of LAA function to normal values after cardioversion may be more rapid in patients with AFL than in those with AF. This hypothesis also prompted us to perform this study.

Table 2. Serial Changes in Number of Patients With Certain Transesophageal Echocardiographic Indexes

	Before	Within 24 h	1 Week	2 Weeks
LAAEV				
≤20 cm/s	0	9	2	0
21–30 cm/s	2	4	3	0
31–40 cm/s	6	3	6	2
>40 cm/s	8	0	5	14
SEC	1 (16%)	8 (50%)	3 (19%)	0
Mild	1	5	3	0
Severe	0	3	0	0

LAAEV = left atrial appendage emptying velocities; SEC = spontaneous echo contrast.

Comparison with previous studies. To our knowledge, there is only one study that practically investigated the return of depressed LAA function to normal values after cardioversion of patients with chronic AFL. Sparks et al. (5) evaluated LAA function and SEC by TEE before, immediately after, 30 min after, and three weeks after ablation of chronic AFL in 15 patients. They demonstrated that significant LAA stunning and developed SEC were present until 30 min after ablation. After three weeks of sustained SR, these findings improved, and anticoagulation with warfarin could be discontinued. In this study, we evaluated LAA stunning within 24 h (19 ± 2 h) and one and two weeks after ablation of chronic AFL. Our study lacks the data obtained immediately after, 30 min after, and three weeks after ablation. However, it seems that there are no significant differences between the present study and the study by Sparks et al. (5) with respect to the patient population and the mode of cardioversion. We believe both studies provide complementary information. Accordingly, we hypothesize as follows: 1) significant LAA stunning that occurs immediately after AFL ablation continues from several hours to one week; and 2) forceful LAA contractions resume within two weeks and may continue to improve for three weeks.

Study limitations. Our study has several limitations. The limited sample size may have excluded subgroups of patients at a particularly high risk for the development of thromboembolism in the post-cardioversion period. These patients may have a more delayed recovery of LAA function. Second, we enrolled only patients with pure AFL and obtained echocardiographic data from patients who had maintained SR after ablation. Nevertheless, we may have missed episodes of intermittent AF because both types of arrhythmias may confer similar symptoms and indeed many episodes of AF are asymptomatic (14). Therefore, it is conceivable that episodes of occult AF could contribute to our results. Third, the criteria used to justify discontinuation of anticoagulation in this study (LAAEV >30 cm/s and absence of SEC) were based on well-accepted observations that LAAEV ≤20 cm/s and SEC are independent risk factors for thromboembolism (15,16), but these criteria refer mainly to persistent AF (not to cardioversion or AFL).

With respect to LAAEV, we had some safety margin to LAAEV ≤20 cm/s in this study.

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