Sinus rhythm restoration and arrhythmia noninducibility are major predictors of arrhythmia-free outcome after ablation for long-standing persistent atrial fibrillation: A prospective study

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BACKGROUND The impact of restoring sinus rhythm (SR) by initial ablation in patients with long-standing persistent atrial fibrillation (LSPAF) is not fully established.

OBJECTIVE The purpose of this study was to investigate the prognostic value of SR restoration at the initial procedure and arrhythmia noninducibility at the final repeat procedure for long-term outcome.

METHODS A total of 203 patients (22% female; age 59 ± 9 years) underwent stepwise catheter ablation for LSPAF.

RESULTS The procedural end-point of SR restoration was achieved in 50% of patients. During follow-up (median 48 months) and after 1.7 procedures per patient, 72% of patients were free from arrhythmia off antiarrhythmic drugs. Failure to restore SR was independently predicted by left atrial (LA) long-axis diameter ≥68 mm (relative risk [RR] 1.55, $P = .03$], proportion of high-voltage LA sites <20% (RR 1.62, $P = .02$), and left atrial appendage (LAA) atrial fibrillation cycle length (AFCL) <155 ms (RR 1.5, $P = .05$). Arrhythmia recurrence after the initial procedure was predicted by SR nonrestoration (RR 2.99, $P < .000001$) and LAA AFCL ≥155 ms (RR 1.90, $P = .0002$). Arrhythmia recurrence after the final procedure was predicted by SR nonrestoration at the initial procedure (RR 2.83, $P = .0007$), persistent AF duration ≥24 months (RR 2.74, $P = .002$), LAA outflow velocity <40 cm/s (RR 2.21, $P = .006$), and LAA AFCL ≥155 ms (RR 1.92, $P = .02$). In 115 patients with repeat procedure(s), failure to achieve arrhythmia noninducibility at the final procedure (19% of patients) was associated with arrhythmia recurrence (RR 8.9, $P < .000001$).

CONCLUSION SR restoration at the initial procedure and arrhythmia noninducibility at the last repeat procedure were major predictors of arrhythmia-free outcome after ablation for LSPAF.

KEYWORDS Atrial fibrillation; Long-standing persistent atrial fibrillation; Sinus rhythm restoration; Noninducibility; Outcome

ABBREVIATIONS **AAD** = antiarrhythmic drug; **AF** = atrial fibrillation; **ANOVA** = 1-way analysis of variance; **AT** = atrial tachycardia; **CI** = confidence interval; **CL** = cycle length; **CS** = coronary sinus; **CTI** = cavotricuspid isthmus; **LA** = left atrium; **LAA** = left atrial appendage; **LMI** = lateral mitral isthmus; **LSPAF** = long-standing persistent atrial fibrillation; **LV** = left ventricle; **NT-proBNP** = N-terminal prohormone of brain natriuretic peptide; **PV** = pulmonary vein; **RA** = right atrium; **RR** = relative risk; **SR** = sinus rhythm

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Introduction

Predictors of successful catheter ablation for persistent atrial fibrillation (AF) were investigated primarily in mixed populations of subjects having AF continuous for 7 days to years.[1–6] Limited data are available for patients with purely long-standing persistent AF (LSPAF). Arrhythmogenic substrate progression as a result of continuous AF duration inversely relates with the success rate of restoring sinus rhythm (SR) by ablation and favorable long-term outcome.[2,7] Prior studies in LSPAF patients did not confirm a prognostic value of SR restoration by ablation.[8,9]

The present study sought to identify predictors of (1) failure to restore SR by ablation, (2) long-term AF or atrial tachycardia (AT) recurrence after the initial ablation, and (3) long-term AF/AT recurrence after the final (ie, initial or repeat) ablation in consecutive subjects with LSPAF.

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Methods

Study population

This single-center study analyzed a prospective registry of all 203 consecutive patients who underwent their first AF ablation between July 2006 and December 2011 and met all of the following criteria: (1) age 18–80 years; (2) symptomatic LSPAF lasting >12 months without intervening SR; (3) refractory to oral amiodarone; and (4) resistant to electrical cardioversion or recurrence within 7 days after cardioversion. Patients with tachycardia-induced cardiomyopathy, which was suspected clinically after careful review of medical records, were eligible for the study. Patients with left ventricular (LV) dysfunction and significant coronary artery disease or suspected idiopathic dilated cardiomyopathy were not included. Ethical approval by the Institutional Review Board was obtained, and all patients gave written informed consent.

Preablation examination

Before the initial procedure, transthoracic/transesophageal echocardiography and blood sampling for N-terminal prohormone of brain natriuretic peptide (NT-proBNP) level were performed. Standardized left atrial (LA) and LV diameters were measured. LV ejection fraction was assessed by the Simpson method from the cycle exhibiting maximum LV filling, and left atrial appendage (LAA) outflow velocity was defined as the peak value within the 30-second recording.

Electrophysiologic study, electroanatomic mapping, and ablation

Periprocedural anticoagulation regimen, mapping/ablation technology, and strategy were described in detail elsewhere.[10] In brief, point-by-point ablation with an irrigated-tip catheter (NaviStar ThermoCool, Biosense Webster, Diamond Bar, CA) navigated in preacquired 3-dimensional electroanatomic maps (CARTO, Biosense Webster) of the LA and right atrium (RA) was performed off warfarin, with class I or III antiarrhythmic drugs (AADs) discontinued except for amiodarone, target activated clotting time of 300–400 seconds, irrigation at 20 mL/min, temperature 42°C, and power limit of 35 W (20–25 W inside the coronary sinus [CS]).

Mandatory wide-area pulmonary vein (PV) isolation and ablation of the LA roof, lateral mitral isthmus (LMI), and cavotricuspid isthmus (CTI) were performed in all patients. When AF continued, a stepwise approach (consisting of CS ablation/isolation and additional linear or cluster electrogram-guided ablation) was successively used in the LA and RA. Ablation at the high interatrial septum and along the Bachmann bundle was deferred as the last step in order to minimize the risk of LAA activation delay or isolation.

The stepwise ablation strategy was pursued until AF converted directly into SR or into AT, which was subsequently identified and ablated by activation and entrainment mapping. If ablation failed to restore SR, intravenous propafenone, overdrive pacing, and electrical cardioversion were successively applied. At the end of the procedure, PV isolation was confirmed by the circular catheter (Lasso, Biosense Webster), and efforts were made to achieve bidirectional conduction block (if not already present) at the CTI, LMI, and roof line. LA volumes and bipolar voltage characteristics were derived from electroanatomic maps as described previously.[11] The dominant atrial fibrillation cycle length (AFCL) in the LAA was assessed by averaging multiple consecutive cycles.[3,12]

Postablation management

Low-molecular-weight heparin was administered after the procedure until the resumption of warfarin treatment. Class I or III AADs were discontinued at the 3-month visit in cases of uneventful follow-up. Warfarin was stopped after 6 months in patients with stable SR, preserved LAA function (outflow velocity ≥40 cm/s), and absence of other conditions requiring permanent anticoagulation.

At repeat procedures, PVs were reisolated and incidental gaps in linear lesions at the roof line, LMI and CTI were closed, even if passive in the mechanism of recurrent arrhythmia. Arrhythmia noninducibility was tested by atrial incremental pacing up to 300 bpm for at least 5 times after each arrhythmia termination in all patients. Isoproterenol and adenosine were used in 63 and 43 patients who were not inducible by pacing.

Follow-up

Patients were seen in the outpatient department every 3 months during the first year and every 6 months thereafter. ECG documentation consisted of 12-lead ECG and 24-hour Holter monitoring before each visit. In addition, 3-week transtelephonic episodic ECG monitoring was performed twice per year up to 2 years and annually thereafter. Arrhythmia recurrence after the 3-month blanking period included ECG-documented AF/AT as well as palpitations suggestive of AF/AT lasting >30 seconds unless arrhythmia was objectively excluded. "Good arrhythmia control" status at the end of follow-up was defined as AF/AT absence in the past 6 months and ≤1 electrical/pharmacologic cardioversion in the past 2 years.

Statistical analysis

Continuous variables are expressed as mean ± SD or median with interquartile range. Categorical variables are expressed as percentages. The relationship of continuous variables was analyzed by Pearson correlation, and differences between subgroups of patients were compared by 1-way or multifactorial analysis of variance (ANOVA). Association of all available clinical and procedure-related characteristics with 3 end-points (SR nonrestoration by ablation, and AF/AT recurrence after the initial ablation and after the final ablation) were investigated by linear or Cox proportional hazards regression models, as appropriate. For this purpose, continuous variables were dichotomized at the median or other clinically meaningful value. All factors, which were