A critical decrease in dominant frequency and clinical outcome after catheter ablation of persistent atrial fibrillation

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BACKGROUND Termination of persistent atrial fibrillation (AF) by radiofrequency ablation (RFA) is associated with a high probability of freedom from AF but requires extensive ablation and long procedure times.

OBJECTIVE The purpose of this study was to determine whether a critical decrease in the dominant frequency (DF) of AF is a sufficient endpoint for RFA of persistent AF.

METHODS Antral pulmonary vein isolation (APVI) followed by RFA of complex fractionated atrial electrograms (CFAEs) in the atria and coronary sinus was performed in 100 consecutive patients with persistent AF. The DF of AF in lead V1 and in the coronary sinus was determined by fast Fourier transform (FFT) analysis at baseline and before termination of AF to identify a critical decrease in DF predictive of sinus rhythm after RFA.

RESULTS A ≥11% decrease in DF had the highest accuracy in predicting freedom from atrial arrhythmias, with a sensitivity of 0.71 and a specificity of 0.82 ($P < .001$). At a mean follow-up of 14 ± 3 months after one ablation procedure, sinus rhythm was maintained off antiarrhythmic drugs in 8/35 (23%) and 20/26 (77%) of patients with a <11% and ≥11% decrease in DF, respectively ($P < .001$). Sinus rhythm was maintained in 24/39 patients (62%) in whom RFA terminated AF. The duration of RFA and total procedure time were longer in patients with AF termination (95 ± 23 and 358 ± 87 minutes) than in patients with a <11% decrease in the DF (77 ± 16 and 293 ± 70 minutes) or ≥11% decrease in DF (80 ± 17 and 289 ± 73 minutes), respectively ($P < .01$). Among the variables of age, gender, left atrial diameter, duration of AF, left ventricular ejection fraction, duration of RFA, a ≥11% decrease in DF, and termination of AF, a ≥11% decrease in DF (odds ratio = 9.89, 95% confidence interval [CI] 2.84–34.47) and termination during RFA (OR = 4.38, 95% CI 1.50–12.80) were the only independent predictors of freedom from recurrent atrial arrhythmias.

CONCLUSION In a retrospective analysis of consecutive patients with persistent AF, a decrease in the DF of AF by 11% in response to APVI and ablation of CFAEs was associated with a probability of maintaining sinus rhythm that was similar to that when RFA terminates AF.

KEYWORDS Atrial fibrillation; Catheter ablation; Endpoint; Dominant frequency

ABBREVIATIONS **AF** = atrial fibrillation; **APVI** = Antral pulmonary vein isolation; **CI** = confidence interval; **CFAE** = complex fractionated atrial electrogram; **CS** = coronary sinus; **DF** = dominant frequency; **EF** = ejection fraction; **FFT** = fast Fourier transform; **LA** = left atrium; **LV** = left ventricle; **PV** = pulmonary vein; **RFA** = radiofrequency ablation; **ROC** = receiver operator characteristics

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Termination of atrial fibrillation (AF) during radiofrequency ablation (RFA) of paroxysmal or persistent AF is predictive of freedom from recurrent AF.[1–5] However, termination of persistent AF usually requires extensive ablation beyond the pulmonary veins (PVs), including ablation of complex fractionated atrial electrograms (CFAEs) and multiple linear lesions.[6] Extensive ablation is associated with a long procedure duration, radiation exposure,[4] proarrhythmia,[4,7] risk of collateral damage, and compromise of left atrial (LA) transport function.[8]

It is not clear whether termination of AF is necessary for optimal clinical efficacy or whether a critical reduction in the dominant frequency (DF) of AF might suffice as an endpoint. The purpose of this study was to determine whether a critical decrease in the DF of persistent AF is predictive of a clinical efficacy similar to that observed after termination of AF during RFA.

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Table 1 Clinical characteristics

	Study subjects (n = 100)
Age, years	60 ± 9
Gender, male/female	87/13
Duration of AF, years[a]	5.1 (±95% CI = 4.23–6.06; median = 4; interquartile range = 3)
LA size, mm	47 ± 5
Left ventricular ejection fraction	0.54 ± 0.09
Structural heart disease	43 (43)
Ischemic heart disease	19 (19)
Nonischemic cardiomyopathy	5 (5)
Hypertensive heart disease	29 (29)
Baseline DF in the CS, Hz	5.93 ± 0.77
Baseline DF in lead V1, Hz	6.06 ± 0.80

[a]Data are shown as mean ± standard deviation except for the duration of AF, which was presented as mean ± 95% CI and median with interquartile range as data were not normally distributed. Percent values are shown in parentheses.

Methods

Study subjects

The subjects of this study were 100 consecutive patients with persistent AF who underwent antral PV isolation (APVI) followed by ablation of CFAEs in the left and right atria and coronary sinus (CS). The clinical characteristics of the patients are shown in Table 1. Patients who had undergone a prior ablation procedure for AF were excluded from this study.

Electrophysiologic study and catheter ablation

The study protocol was approved by the Institutional Review Board, and all patients provided informed written consent. The electrophysiological studies were performed in the fasting state. All antiarrhythmic drug therapy was discontinued 4–5 half-lives before the procedure, except for amiodarone, which was discontinued 8–12 weeks beforehand. Vascular access was obtained through a femoral vein. A steerable decapolar catheter (Biosense Webster, Diamond Bar, CA) was positioned in the CS throughout the procedure. After two transseptal punctures, systemic anticoagulation was achieved with intravenous heparin to maintain an activated clotting time of 300–350 seconds. The PVs were mapped with a decapolar ring catheter (Lasso, Biosense Webster). An open-irrigation, 3.5-mm-tip deflectable catheter (Thermocool, Biosense Webster) was used for mapping and ablation. Bipolar electrograms were displayed and recorded at filter settings of 30–500 Hz during the procedure (EPMed Systems, West Berlin, NJ).

The LA and PVs were constructed with a three-dimensional electroanatomical mapping system (Carto, Biosense-Webster). Conscious sedation was achieved with fentanyl and midazolam after barium swallow to visualize the esophagus.[9]

The ablation strategy consisted of APVI followed by ablation of CFAEs. The endpoint of ablation was termination of AF or elimination of all identifiable target electrograms, at the discretion of the primary operator.[5,10] There was no time limit on the duration of ablation. CFAEs were defined as electrograms with a cycle length <120 ms or shorter than in the CS or that were fractionated or displayed continuous electric activity.[5,10] Radiofrequency energy was delivered at a power of 25–35 W, a maximum flow rate of 30 mL/minute, and a maximum temperature of 45°C. Whenever AF converted to an atrial tachycardia, the tachycardia was mapped and ablated. An atrial tachycardia was defined by (1) discrete and monomorphic P waves on the electrocardiogram; (2) regularity of the electrograms recorded in the LA and CS with <20 ms variability in cycle length; and (3) stable activation sequence. Electrical cardioversion was used to restore sinus rhythm if AF or atrial tachycardia was still present after ablation.

Digital signal processing and data analysis

All patients presented to the laboratory in AF. Electrograms were recorded in lead V1 and in the CS for 60 seconds and were used for subsequent analysis. Those electrograms were processed offline in the MatLab environment (MathWorks, Inc., Natick, MA) using custom software. As described elsewhere, the QRS or QRST complexes (in V1) were subtracted. First, digitized bipolar electrograms, sampled for 60 seconds at 1000 Hz (60,000 points), underwent the preprocessing steps of band-pass filtering at 40–250 Hz, rectification, and low-pass filtering at 20 Hz. Then the discrete Fourier transform of the preprocessed signal was computed using the fast Fourier transform (FFT) algorithm to analyze the 0.5–80 Hz spectral band. An estimate of the signal spectrum was obtained by computing the periodogram, which is the modulus squared of the discrete Fourier transform. The frequency resolution was 0.017 Hz. The DF was defined as the frequency of the highest peak of the smoothed periodogram in the interval of 0.5–20 Hz.[11,12]

Lead V1 was used in the primary data analysis because it provides a more global representation of atrial activation than the CS and because CS electrograms were excluded from analysis whenever radiofrequency energy was applied within the CS (n = 61). However, to demonstrate the correlation between lead V1 and intracardiac electrograms recorded in the CS, analyses based on CS electrograms were also provided. The primary objective was to determine the role of a relative change (%) in DF of AF in lead V1 from baseline to just before termination of AF (by cardioversion or during RFA) as a predictor of clinical outcome after RFA.

Postablation care and follow-up

Among the 100 patients, the only complication was a groin hematoma. All patients were monitored and anticoagulated during overnight hospitalization then discharged on warfarin and low molecular weight heparin if the international normalized ratio (INR) was <2.0 during the procedure. The latter was continued until the INR was ≥2.0. Patients were seen in an outpatient clinic 3 months after the procedure and every 3–6 months thereafter. They were instructed to con-