Electrogram organization predicts left atrial reverse remodeling after the restoration of sinus rhythm by catheter ablation in patients with persistent atrial fibrillation

Kentaro Yoshida, MD,* Hiroshi Tada, MD,* Kuniomi Ogata, M.Eng,† Yukio Sekiguchi, MD,* Takeshi Inaba, RDCS,* Yoko Ito, MD,* Yoko Sato, MD,* Akira Sato, MD,* Yoshihiro Seo, MD,* Akihiko Kandori, PhD,† Kazutaka Aonuma, MD*

*From the *Division of Cardiovascular Medicine, University of Tsukuba, Tsukuba, Japan, and †Central Research Laboratory, Hitachi Ltd, Kokubunji, Japan.*

BACKGROUND Despite the informative nature of atrial fibrillation (AF) electrograms, electrophysiological aspects of predicting reversal of structural remodeling of the left atrium (LA) have not been evaluated.

OBJECTIVES To identify predictors of reverse remodeling after restoration of sinus rhythm by catheter ablation in patients with persistent AF.

METHODS This study included 90 patients with persistent AF and enlarged LA (left atrial volume indexed to body surface area [LAVi] $\geq$32 mL/m^2). LAVi was measured by echocardiography before ablation and 12 months after sinus rhythm restoration. We divided 73 (81%) patients free from recurrences into 2 groups according to reduction in LAVi: responders, reduction $\geq$23% (n = 35); nonresponders, reduction <23% (n = 38). Serological testing and electrophysiological characteristics on electrocardiogram and magnetocardiogram were analyzed.

RESULTS LAVi decreased from 43 $\pm$ 12 to 27 $\pm$ 7 mL/m^2 in responders and from 37 $\pm$ 8 to 33 $\pm$ 8 mL/m^2 in nonresponders. Higher LAVi at baseline (P = .01), lower age (59 $\pm$ 7 years vs 63 $\pm$ 7 years; P <.05), higher brain natriuretic peptide level (median = 92, interquartile range [IQR] = 98 pg/mL vs median = 60, IQR = 64 pg/mL; P = 0.01), higher atrial natriuretic peptide level (median = 73, IQR = 74 pg/mL vs median = 54, IQR = 70 pg/mL; P = .02), and higher organization index of AF signals (0.51 $\pm$ 0.11 vs 0.42 $\pm$ 0.09; P = .0001) were observed in responders. There was a linear correlation between organization index and % reduction in LAVi (R = 0.63; P <.0001). Multiple linear regression analysis showed relations between reverse remodeling and age (β = −0.28; P = .002), atrial natriuretic peptide level (β = 0.21; P = .03), and organization index (β = 0.53; P <.0001).

CONCLUSIONS Electrogram organization was a robust predictor of reverse remodeling of the enlarged LA after sinus rhythm restoration by catheter ablation in patients with persistent AF.

KEYWORDS Atrial fibrillation; Catheter ablation; Reverse remodeling; Organization; Magnetocardiogram

ABBREVIATIONS **AF** = atrial fibrillation; **ANP** = atrial natriuretic peptide; **BNP** = brain natriuretic peptide; **CS** = coronary sinus; **DF** = dominant frequency; **ECG** = electrocardiography; **IQR** = interquartile range; **LA** = left atrial; **LAVi** = LA volume indexed to body surface area; **MCG** = magnetocardiography; **PV** = pulmonary vein; **OI** = organization index

(Heart Rhythm 2012;9:1769–1778)

Introduction

Left atrial (LA) size has been established as a prognostic marker of cardiovascular morbidity and stroke.[1,2] One cause of LA enlargement is atrial fibrillation (AF).[3–6] Studies have shown reduction in LA enlargement and functional improvement after restoration of sinus rhythm (reverse remodeling) with certain medications or radiofrequency catheter ablation.[7] However, reversal of structural remodeling occurs to different degrees in contrast to uniform reversal of electrical remodeling.[7–9]

Patients with drug-resistant, symptomatic AF are suitable candidates for catheter ablation because their quality of life improves appreciably after successful treatments with acceptable complication rates.[10] However, approximately 40% of the patients with AF are asymptomatic.[11] Reduction in LA volume after restoration of sinus rhythm, which may lead to improvement in LA function and exercise tolerance,[12,13] less likelihood of thrombus formation,[14] and less susceptibility to further atrial arrhythmias,[4,8] appears to justify a more aggressive clinical approach such as catheter ablation even in less symptomatic patients. Although a study reported echocardiographic predictors, such as LA strain and strain rate, of LA reverse remodeling after ablation,[8] their applications are limited to use during sinus rhythm and therefore may be used mostly in patients with paroxysmal AF. Despite the informative nature of AF elec-

Address for reprint requests and correspondence: Dr Kentaro Yoshida, MD, Division of Cardiovascular Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8575, Japan. E-mail address: kentaroyo@nifty.com.

1547-5271/$ -see front matter http://dx.doi.org/10.1016/j.hrthm.2012.06.033

trograms, electrophysiological aspects of predicting reverse remodeling remain unevaluated. The present study was designed to evaluate with the noninvasive methods of electrocardiography (ECG) and magnetocardiography (MCG) whether characteristics of AF electrograms can predict reverse remodeling after restoration of sinus rhythm by catheter ablation in patients with an enlarged left atrium resulting from persistent AF.

Methods

Study subjects

The study subjects comprised 90 consecutive patients with an enlarged left atrium of ≥32 mL/m^2 who were referred for LA ablation of persistent AF.[3] All patients presented to hospital in AF. Transthoracic echocardiography (Vivid 7, GE Healthcare, Horten, Norway) was performed during AF 1 day before the ablation procedure and during sinus rhythm 12 months after the final ablation procedure by sonographers blinded to any electrophysiological data. LA volumes were measured on apical 2- and 4-chamber views during end-systole with the biplane method.[15] Patients with structural heart disease or a prior ablation procedure for AF were excluded from this study. All antiarrhythmic drug therapy was discontinued 4–5 half-lives before the procedure except for amiodarone, which was discontinued 8 weeks beforehand. The study protocol was approved by the local Institutional Review Board, and all patients provided their informed written consent.

MCG and ECG analyses

Patients underwent MCG during AF 1 day before ablation. MCG methodology was described in detail previously.[16] Briefly, we used an MCG system (MC-6400, Hitachi High-Technologies Corporation, Tokyo, Japan) with 64 sensors to measure the normal component of the magnetic field. The sensors were arranged in an 8 × 8 matrix with 25-mm pitch and 175 × 175-mm measurement area. MCG signals for each subject in the resting state were recorded from the frontal and back planes in a magnetically shielded room. Relative location of the sensors to the patient's body is shown in Figure 1A. The sampling rate was 1 kHz, and the measurement period was 1 minute.[17] MCG signals were passed through a bandpass filter (0.1–50 Hz) and power line noise filter (50 Hz). ECG leads II, V_1, and V_5 were simultaneously recorded throughout MCG recording.

To analyze the MCG signals generated from an atrial electrical activation, we subtracted the QRS-complex and T-wave signals from the measured MCG signals by using the template QRS-T waveform.[16] We also calculated the power spectrum by using fast Fourier transform techniques: the highest peak of the power spectrum in the 0.5- to 20-Hz range was defined as the dominant frequency (DF). To quantify the organization of AF electrograms, the organization index (OI) was calculated as the ratio of the total area of the spectrum under the first 5 harmonic peaks to the total area of the spectrum.[18]

We defined "mean OI" as the mean value of 64 OIs in a given plane and "highest OI" as the highest value among 64 OIs in a given plane (Figure 1B). Similarly, we defined "mean DF" as the mean value of 64 DFs in a given plane and "DF with highest OI" as the DF in the channel with the highest OI among 64 channels. Channels with a DF beyond the biological range of 3–12 Hz were excluded from further analysis (Figure 1B).[19]

The same fast Fourier transform techniques were applied to the ECG electrograms (Figure 1C). Furthermore, the amplitude of the fibrillatory waves (F waves) was measured with electronic calipers in leads II, V_1, and V_5. Ten discrete F waves were selected during a period of slow ventricular rate and were measured manually from peak to trough.[20] Maximal amplitude in each lead is reported in the present study.

Electrophysiologic study and catheter ablation

A 7-F 14-pole dual-site mapping catheter (Irvine Biomedical, Inc, Irvine, CA) was positioned in the coronary sinus (CS) and low lateral wall of the right atrium throughout the procedure. Three long sheaths (SL0, AF Division, St Jude Medical, Minnetonka, MN) were advanced into the left atrium. Following pulmonary vein (PV) angiography, 2 decapolar ring catheters (Lasso, Biosense Webster, Diamond Bar, CA) were placed in the superior and inferior PVs on 1 side at a time. 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 (CardioLab System, Pruka Engineering, Houston, TX).

The ipsilateral PV antrum was circumferentially ablated under fluoroscopic, electrogram, and CARTO (Biosense Webster) guidance. PV isolation was followed by ablation of complex fractionated electrograms in the left atrium and within the CS. The following sites were preferentially targeted given their demonstrated benefit in AF termination: inferior left atrium over the CS, anterior and posterior aspects of the LA appendage, LA septum, and the CS itself. Electrical cardioversion was used to restore sinus rhythm if AF or atrial tachycardia was still present after ablation. End point of the ablation procedure was termination of AF or completion of ablation strategy (PV isolation and LA/CS defragmentation). Radiofrequency energy was delivered at a power of 20–35 W, maximum irrigation flow rate of 30 mL/min, and maximum temperature of 42°C.

Postablation care and follow-up

Patients were discharged on warfarin ≥5 days after ablation. Patients were seen in an outpatient clinic 2 and 6 weeks after hospital discharge and every 2 months thereafter. Holter (DSC-3300, Nihon Kohden, Tokyo, Japan) or event recorder (HCG-901, Omron, Kyoto, Japan) recordings were undertaken before the outpatient visits, and treatment success was defined as freedom from all atrial tachyarrhyth-