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Pre-Procedural Serum Atrial Natriuretic Peptide Levels Predict Left Atrial Reverse Remodeling After Catheter Ablation in Patients With Atrial Fibrillation

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ABSTRACT

OBJECTIVES This study aimed to investigate the role of atrial natriuretic peptide (ANP) levels to predict left atrial (LA) reverse remodeling in atrial fibrillation (AF) patients.

BACKGROUND Although LA reverse remodeling after radiofrequency catheter ablation (RFCA) for AF was reported to be associated with favorable outcomes and improvement of LA and left ventricular function, the predictor has not been extensively evaluated.

METHODS This study included 104 consecutive patients who underwent RFCA for AF. All patients underwent multidetector computed tomography examination and laboratory tests, including measurement of ANP, plasma B-type natriuretic peptide (BNP), and high-sensitivity C-reactive protein (hs-CRP) levels before and 6 months after RFCA. The study population was divided according to the extent of the decrease in the LA volume index at follow-up; responders were defined as patients who exhibited a ≥15% decrease in the LA volume index.

RESULTS At follow-up, 49 patients (47%) were classified as responders. Pre-procedural serum ANP and BNP levels were significantly higher in the responders than in the nonresponders (both $p < 0.01$). In the responders, a significant decrease was observed in the log ANP, log BNP, and log hs-CRP levels from baseline to follow-up (all $p < 0.01$). Multivariate linear regression analysis revealed that log ANP levels before RFCA and maintenance of sinus rhythm during follow-up were independent predictors of LA reverse remodeling (both $p < 0.01$).

CONCLUSIONS In this study, 47% of the patients exhibited LA reverse remodeling after RFCA for AF, with a concomitant improvement in serum ANP, BNP, and hs-CRP levels. The pre-procedural ANP level and maintenance of sinus rhythm were independently associated with LA reverse remodeling. (J Am Coll Cardiol EP 2016;2:151–8)
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Atrial fibrillation (AF) is the most common cardiac arrhythmia encountered in clinical practice and is associated with atrial remodeling; the hallmark of structural remodeling is atrial dilatation (1,2). Radiofrequency catheter ablation (RFCA) is considered a reasonable treatment option for patients with symptomatic drug-refractory AF (3), and successful RFCA is known to be associated with a decrease in left atrial (LA) volume (reverse remodeling) (4–6). However, the degree of reverse remodeling varies among individuals (7,8), and this predictor has not been evaluated extensively. Because LA reverse

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

ANP = atrial natriuretic peptide

BNP = B-type natriuretic peptide

ECG = electrocardiography

hs-CRP = high-sensitivity C-reactive protein

LA = left atrium

LV = left ventricle

MDCT = multidetector computed tomography

PV = pulmonary vein

RFCA = radiofrequency catheter ablation

remodeling leads to subsequent improvement in the LA (9) and left ventricular (LV) function (10), prediction of reverse remodeling is of crucial importance.

Atrial natriuretic peptide (ANP) is a hormone released from atrial myocytes in response to volume or pressure overload (11). Although elevated plasma ANP levels are frequently observed in AF patients (12–14), data indicate that ANP levels are low in patients with advanced atrial fibrosis (15,16). Thus, we hypothesized that elevated ANP levels in AF patients partially reflect the viability of LA myocytes, which may result in a considerable decrease in LA volume after RFCA. This study aimed to investigate the role of ANP levels to predict LA reverse remodeling in patients who underwent RFCA for AF.

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METHODS

STUDY POPULATION. The study population consisted of 104 consecutive patients who had paroxysmal (n = 65) and persistent AF (n = 39) refractory to antiarrhythmic treatment and who were referred to undergo RFCA first. The exclusion criteria were: 1) history of myocardial infarction; 2) moderate or severe valvular disease; 3) dilated or hypertrophic cardiomyopathy; 4) thyroid dysfunction; and 5) renal insufficiency (serum creatinine level ≥1.5 mg/dl). AF was defined as paroxysmal when the arrhythmia self-terminated within 7 days and as persistent when the AF episode persisted for 7 days, or pharmacological or electrical cardioversion was required to terminate the arrhythmia (17). Self-reported AF burden was evaluated on the basis of a modified arrhythmia frequency and severity scale, from 1 to 10 points for each frequency and duration of AF episodes (range 2 to 20) (18,19). All patients underwent multidetector computed tomography (MDCT) examination 7 ± 3 days before and 6 months after RFCA. Laboratory tests, including measurement of ANP, plasma B-type natriuretic peptide (BNP), and high-sensitivity C-reactive protein (hs-CRP) levels were performed before RFCA on the day of ablation and at 6-month intervals after RFCA. This study was approved by the institutional review board of Baba Memorial Hospital, and written informed consent was obtained from all patients.

MEASUREMENT OF ANP, BNP, AND hs-CRP. Blood samples were collected from the antecubital vein after patients rested in the supine position for ≥30 min. All samples were drawn in the morning before taking medication. Samples were collected in tubes containing 1.25 mg/ml of ethylenediaminetetraacetic acid and a protease inhibitor, aprotinin 500 KIU/ml (for measurement of ANP and BNP). The plasma was separated by centrifugation (at 2,500 rpm) for 10 min at 20°C and stored at −70°C until measurement. Serum ANP concentration was measured with the HISCL ANP immunoassay (Shionogi, Osaka, Japan), and the BNP concentration was measured with the ARCHITECT BNP immunoassay (Abbott Laboratories, Abbott Park, Illinois). hs-CRP was analyzed with the CardioPhase hs-CRP assay (Siemens Healthcare Diagnostics, Marburg, Germany).

SCAN PROTOCOL AND INTERPRETATION OF CT FINDINGS. MDCT examination was performed using the Aquilion 64-detector scanner (Toshiba Medical Systems, Tokyo, Japan) before and 6 months after RFCA. A retrospective electrocardiography (ECG)-gated, contrast-enhanced scan was performed with a slice collimation of 64 × 0.5 mm, tube rotation time of 400 to 500 ms (as determined by the heart rate), tube voltage of 120 kV, and tube current of 350 to 500 mA depending on patient size. Automated detection of peak enhancement in the ascending aortic arch was used for timing of the scan. For contrast-enhanced scans, 50 to 80 ml of a nonionic contrast agent (Iopamidol 370, Hikari Co., Tokyo, Japan) was injected intravenously at a flow rate of 4.0 to 5.5 ml/s, followed by 40 ml of saline solution at a rate of 5 ml/s. The raw data were reconstructed using algorithms optimized for ECG-gated multislice spiral reconstruction. Images were transferred to a commercially available workstation, SYNAPSE VINCENT (Fujifilm Medical Co., Tokyo, Japan). All MDCT analyses were performed by experienced physicians blinded to other information. The following parameters were assessed.

1. The LA volume was measured using Simpson's rule at end-systole. Pulmonary veins (PVs) and the LA appendage were carefully excluded.
2. Manual planimetry of the endocardial and epicardial LV borders (to define the LV myocardial area) was performed at end-diastole, on short- and long-axis images. The LV volume was calculated using the modified Simpson's method, in which the sum of the cross-sectional areas was multiplied by the sum of slice thicknesses. The LV papillary muscles were excluded from the mass measurement. The LV mass was calculated using the following formula: 1.05 g/ml × LV volume.

The LA volume and LV mass were indexed for body surface area.