Left Atrial Reverse Remodeling After Catheter Ablation of Nonparoxysmal Atrial Fibrillation in Patients With Heart Failure With Reduced Ejection Fraction

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The efficacy of catheter ablation (CA) of nonparoxysmal atrial fibrillation (PAF) in patients with left ventricular systolic dysfunction is controversial. We investigated the outcomes of CA for non-PAF in patients with reduced left ventricular ejection fraction (LVEF) and the impact of early left atrial (LA) reverse remodeling on these outcomes. A total of 251 consecutive patients who underwent CA for non-PAF were divided into 2 groups (reduced: preoperative LVEF ≤55%, LVEF: 46.5 ± 8.7%, n = 63; normal: >55%, 65.8 ± 5.8%, n = 188). We analyzed the 4-year atrial fibrillation- or atrial tachycardia (AT)-free survival rate and assessed changes in LVEF, hemodynamics, and LA reverse remodeling at the end of a 90-day blanking period. We also evaluated LA reverse remodeling in patients with and without recurrence. The atrial fibrillation- or AT-free survival rates were similar (reduced vs normal 48% vs 42%, p = 0.32). The reduced group exhibited significant LVEF improvement (before vs after, 46.5 ± 8.7% vs 58.4 ± 11.5%, p <0.001), reduced mitral regurgitation, and spectral tissue Doppler-derived index, and had greater percent maximum left atrial volume reduction (reduced vs normal 25.3 ± 18.2% vs 19.3 ± 16.2%, p = 0.014). Percent maximum left atrial volume reduction was greater in patients without recurrence (with recurrence vs without recurrence 17.3 ± 16.7% vs 25.4 ± 16.1%, p <0.001). In conclusion, the efficacy of non-PAF CA in patients with reduced LVEF was comparable with that in patients with normal LVEF. Greater LA reverse remodeling in these patients suggests an association with a reduced recurrence rate. **(Am J Cardiol 2018;■■:■■–■■■■–■■)**

Atrial fibrillation (AF) and congestive heart failure can interact with each other in a vicious cycle.[1–3] Recently, several randomized controlled trials enrolling patients with left ventricular (LV) systolic dysfunction demonstrated that catheter ablation (CA) for nonparoxysmal atrial fibrillation (PAF) improved LV systolic function, congestive heart failure symptoms, and prognosis compared with antiarrhythmic drugs (AADs).[4–8] However, the efficacy of CA for non-PAF in patients with LV systolic dysfunction is controversial.[9–12] To investigate the efficacy of CA in patients with LV systolic dysfunction, we divided a cohort of patients who underwent CA for non-PAF into groups with reduced and normal left ventricular ejection fraction (LVEF) and compared long-term outcomes, improvement in LVEF and hemodynamics, and the amount of left atrial (LA) reverse remodeling. In addition, we investigated the amount of LA reverse remodeling in patients with and without recurrence among the entire study population.

Methods

Of 371 consecutive patients who underwent radiofrequency CA of non-PAF in Sakurabashi-Watanabe Hospital from June 2010 to December 2013, we enrolled 251 patients according to the following criteria: (1) successful pulmonary vein antrum isolation; (2) follow-up after CA for >1 year; (3) no repeat CA within a 90-day blanking period; (4) availability of complete echocardiography and multidetector computed tomography (MDCT) datasets before and after initial CA; and (5) preprocedure echocardiography study performed in AF rhythm and persistence of AF rhythm confirmed just before CA. Based on the preoperative LVEF, patients were divided into 2 groups: the reduced LVEF group (LVEF ≤55%, n = 63) and the normal LVEF group (LVEF >55%, n = 188). First, we investigated AF- or atrial tachycardia (AT)-free survival rate over 4 years after single and multiple CA procedures. Next, we analyzed changes in New York Heart Association (NYHA) functional class and structural and hemodynamic changes by echocardiography after initial CA. We then assessed for LA reverse remodeling using the parameters of left atrial volume (LAV) measured by MDCT after initial CA. The

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parameters were maximum left atrial volume (LAV_{max}), minimum left atrial volume (LAV_{min}), left atrial emptying fraction (LAEF) ($[LAV_{max} - LAV_{min}]/[LAV_{max}] \times 100$) and percent maximum left atrial volume ($\%LAV_{max}$) reduction ($[\text{preoperative } LAV_{max}] - [\text{postoperative } LAV_{max}]/[\text{preoperative } LAV_{max}] \times 100$). Finally, we compared the amount of LA reverse remodeling in patients with and without recurrence among the entire study population. The protocol was approved by the institutional review board at Sakurabashi Watanabe Hospital, and all patients gave informed consent for the use of their data.

In CA procedures, we placed a 6-Fr decapolar catheter in the coronary sinus and a 7-Fr decapolar catheter in the superior vena cava and the right atrium. The double or the single lasso technique was used. We used an irrigated ablation catheter with a 3.5-mm tip (Navistar Thermocool; Biosense Webster, Diamond Bar, CA). Radiofrequency energy was delivered for 20 to 30 seconds at each point: up to 35 W, with a temperature limit of 43°C. Pulmonary vein antrum isolation (defined as abolition or dissociation of pulmonary vein potentials) was guided by either fluoroscopy or 3-dimensional mapping. We also attempted to ablate nonpulmonary vein premature atrial contractions if they initiated AF, and targeted atrial flutter coexisting with AF. Superior vena cava isolation, linear ablation of cavotricuspid isthmus, LA roof, LA bottom, mitral valve isthmus, and/or complex fractionated atrial electrography were performed at the discretion of the operator.[13]

Preprocedure echocardiographic data were obtained no more than 1 month before CA. Postprocedure data were obtained 4.9 ± 1.8 months after CA. LVEF was quantified from LV end-diastolic dimensions and systolic dimensions. We recorded tissue Doppler images from the apical 4-chamber view and measured septal e' on the pulse-wave Doppler spectrum averaging 5 consecutive beats. We measured transmitral E as an average of 5 consecutive cardiac cycles and calculated spectral tissue Doppler-derived index (E/e')[14] as the parameter of LV end-diastolic pressure. We scored the severity of mitral regurgitation using the Sellers grading system (none, I, II, III, and IV). All data were obtained by trained observers who were blinded to the ablative outcome.

Within 1 month before and 3 months after CA, patients underwent 256-slice MDCT (Brilliance iCT; Philips Medical Systems, Cleveland, OH). Retrospective electrocardiogram-gated data acquisition was performed in a single breath-hold with the field of view from the level of 20 mm above the split of the pulmonary artery to the apex using a bolus administration of contrast medium (iopamidol 370 mg-iodine/ml, 1 ml/kg; Bayer, Osaka Yakuhin, Osaka, Japan). Ten datasets of axial images with 0.7 mm reconstructed at 5% of the R-R interval were transferred to a commercially available workstation. LAV_{max} and LAV_{min} were measured over 1 cardiac cycle by an independent cardiologist using a semiautomated volumetric segmentation.

After CA, all patients were hospitalized with continuous rhythm monitoring for 3 days. Prescription of AADs was determined by the attending physician. We directed patients to check their pulse rate and rhythm 3 times a day and to visit the outpatient clinic in case of a relapse of AF or AT. Patients were scheduled for visits to the outpatient clinic 1, 3, 6, 9, and 12 months after CA and every 6 months thereafter. A 12-lead electrocardiogram was obtained at each visit. Holter electrocardiography was performed 3 to 6 months after CA on most patients. Recurrence of AF or AT was defined as recurrent symptoms and/or documented AF or AT on electrocardiogram and Holter electrocardiography. A 90-day blanking period after CA was employed.

In univariate analysis for covariates of interest, independent continuous variables were analyzed using an independent-samples Student *t* test, and categorical variables were analyzed using the chi-square test. To compare data before and after CA, paired continuous variables were analyzed using a paired-samples Student *t* test. For survival analysis, primary end points of AF or AT recurrence were identified using the Kaplan-Meier method with log-rank test. All data were expressed as the mean ± standard deviation. All reported *P* values were 2-sided with a prespecified significance of $p < 0.05$. Analyses were performed using MedCalc software version 16.8.4 (MedCalc Software bvba, Ostend, Belgium).

Results

The present study included 251 patients with non-PAF (persistent: n = 169 [67%], long-standing persistent: n = 82 [33%]). The mean age was 60 ± 10 years and 83% were men. The median follow-up duration was 2.1 years (range 0.25 to 4.0). Baseline characteristic are summarized in Table 1. The reduced group had a higher $CHADS_2$ score and NYHA functional class. The reduced group had a significantly higher frequency of use of diuretics and amiodarone. The reduced group had a higher heart rate, larger LV end-diastolic dimensions and systolic dimensions, and lower LVEF. Of the 63 patients in the reduced group, 7 (11%) had an LVEF of 35%. In the reduced group, 7% had ischemic and 93% had nonischemic origin of LV systolic dysfunction. E/e' was similar between the 2 groups. The percentage of Sellers grade III and IV mitral regurgitations was higher in the reduced group. No differences were observed in parameters for LAV in MDCT. Table 2 lists the details of the CA procedures and complications. Pulmonary vein antrum isolation only (or plus cavotricuspid isthmus) was performed in more than 80% of the patients. The reduced group tended to have less LA linear ablation. Complication rates did not differ between the 2 groups.

As shown in Figure 1 and listed in Table 3, there was no significant difference in AF- or AT-free survival rate after the initial procedure over 4 years. AADs or amiodarone in patients without recurrence did not differ. Of 142 patients with recurrence after the initial procedure, 101 underwent multiple procedures. In Figure 1 and in Table 3, AF or AT survival rate did not differ between the 2 groups after multiple procedures over 4 years, and neither did AAD or amiodarone usage.

In Figure 2, both groups showed LVEF improvement (reduced 46.5 ± 8.7% vs 58.4 ± 11.5%, before vs after, $p < 0.001$; normal 65.8 ± 5.8% vs 68.4 ± 6.9%, $p < 0.001$). The percentage of patients with NYHA functional class ≥II decreased in both groups after initial CA (reduced 73% vs 11%, before vs after, $p < 0.001$; normal 51% vs 9%, $p < 0.001$) (Figure 2). In Figure 3, heart rate was decreased in both groups (reduced 97 ± 21 beats/min vs 71 ± 14 beats/min, before vs after, $p < 0.001$; normal 87 ± 22 beats/min vs 73 ± 15 beats/min, $p < 0.001$). E/e' improved only in the reduced group (11.1 ± 5.1 vs 9.3 ± 4.4, before vs after, $p = 0.001$), whereas