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Original article

Impact of catheter ablation of atrial fibrillation on long-term clinical outcomes in patients with heart failure

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ABSTRACT

Background: Heart failure (HF) promotes atrial fibrillation (AF) and AF worsens HF. This study aimed to investigate the long-term clinical outcomes after AF ablation in patients with HF.
Methods and results: A total of 106 consecutive HF patients, including 51 (48.1%) with a reduced left ventricular ejection fraction (LVEF) (HFrEF) and 55 (51.9%) with a preserved LVEF (HFpEF), underwent AF ablation. All patients underwent successful pulmonary vein antrum isolation, and substrate modification was added in 38 (35.8%). The mean follow-up period was 32.4 ± 18.6 months, and mean number of procedures was 1.4 ± 0.5 per patient. Low-dose antiarrhythmic drugs were combined in 29 (27.3%) patients. Freedom from recurrent atrial arrhythmias (ATa), HF-related hospitalizations, and the composite endpoint (all-cause death, stroke, HF-related hospitalizations) at 3 years was 88.7%, 97.6%, and 97.6% in HFrEF patients, and 79.3%, 96.2%, and 91.8% in HFpEF patients, respectively. LVEF normalization (≥50%) was observed in 37 (72.5%) HFrEF patients post-ablation, and a smaller LV diastolic diameter (LVDd) was the sole predictor [odds ratio (OR) = 0.863; 95% confidence interval (CI) = 0.779–0.955, $p = 0.005$]. Shortening of the LVDd (≥5 mm) was observed in 16 (29.1%) HFpEF patients post-ablation, and no recurrence after the initial procedure was the sole predictor (OR = 6.229; 95% CI = 1.524–25.469, $p = 0.011$).
Conclusions: Catheter ablation of AF could be one of the important therapeutic options in the management of patients with HF combined with AF regardless of the type of HF.

Introduction

Hospital admissions for heart failure (HF) have been increasing over the past decade due to an aging population as well as longer survival of patients with chronic heart disease. HF comprises a wide range of patients, from those with a preserved left ventricular ejection fraction (LVEF) (HFpEF) to those with a reduced LVEF (HFrEF), and the proportion of patients with HFpEF ranges from 22% to 73% [1]. Atrial fibrillation (AF) is present in up to 50% of patients with HF regardless of the type of HF, and both are associated with several common predisposing risk factors and a shared pathophysiology. It is widely recognized that HF promotes AF and that AF worsens HF, and the coexistence has a higher morbidity and poor prognosis [1,2]. Restoration of sinus rhythm is expected to improve the clinical outcome in those patients, yet rhythm control with antiarrhythmic drugs (AADs) has not shown any satisfactory results in randomized trials [3], most likely due to the potential adverse effects and insufficient efficacy, which has been supported in the results of the sub-analysis of the AFFIRM trial [4]. Although catheter ablation is another option to maintain sinus rhythm [5,6], currently the evidence of the effect of catheter ablation on HF is limited [7]. Moreover, given the non-negligible incidence of major complications during AF ablation, the data regarding the patients most likely to benefit are essential in selecting the therapeutic options in patients with combined AF and HF. The purpose of the present study was to explore (1) the long-term clinical outcomes after AF ablation in patients with HFrEF and those with HFpEF, and (2) factors predicting reverse remodeling of the left ventricle (LV) after AF ablation in patients with HF.

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Methods

Study population

One hundred and six patients with HF who first underwent catheter ablation for AF in our institution between 2010 and 2015 were enrolled. Since the differentiation of patients with HF based on the LVEF is important due to the different underlying etiologies, demographics, co-morbidities, and response to therapies [1], we divided the patients into 2 groups based on the LVEF. The definition of HF was in accordance with the latest guidelines [1] and HF was classified as HFrEF (LVEF $\leq$ 45%) or HFpEF (LVEF $>$ 45%) according to the LVEF. AF was classified according to the latest guidelines [8]. All patients gave their written informed consent. The study protocol was approved by the hospital's institutional review board. The study complied with the Declaration of Helsinki.

AF ablation procedure

All AADs were discontinued for at least five half-lives prior to the procedure. The patients were effectively anticoagulated for $>$1 month, and transesophageal echocardiography was performed to exclude any atrial thrombi. The ablation was performed under conscious sedation according to the strategy described previously [9–11]. In brief, 100 IU/kg body weight of heparin was administered following the transseptal puncture, and heparinized saline was additionally infused to maintain the activated clotting time at 250–350 s. Pulmonary vein antrum isolation (PVAI) was performed with a double-lasso technique under the guidance of a 3-D mapping system (CARTO 3, Biosense-Webster, Irvine, CA, USA) in all patients. The endpoint of the PVAI was the achievement of bidirectional conduction block between the left atrium (LA) and PVs. Radiofrequency current was delivered point-by-point with a 3.5-mm externally irrigated-tip ablation catheter (Thermocool, Biosense-Webster) with a power of up to 35 W, target temperature of $\leq$38 °C, and irrigation rate of 30 ml/min. The power was limited to 20 W on the posterior wall close to the esophagus. Complete block along the cavo-tricuspid isthmus was created if common atrial flutter was detected before or during the procedure. When an arrhythmogenic superior vena cava (SVC) was identified, an electrical SVC isolation was added. In patients with persistent AF, substrate modification was performed systemically targeting AF termination if AF did not terminate during PVAI as described previously [11]. During the repeat procedure, the previous lesion set was evaluated and consolidated. Then, any identified non-PV foci were eliminated. Stable atrial tachycardias were mapped and ablated by using 3D-activation mapping and entrainment maneuvers.

Heart failure management and echocardiography

All patients were on optimal tolerated medical therapy for HF. Optimal therapy included angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, β-blockers, diuretics, and digoxin when appropriate. In all patients, standard 2D and Doppler echocardiography was performed during the follow-up period. The LVEF was quantified by using a modified biplane Simpson rule in 2- and 4-chamber apical views.

Follow-up

No AADs were prescribed after the procedure in patients with paroxysmal AF, and AADs were prescribed during a 3-month of blanking period and the continuation was determined by the operator's discretion in patients with persistent AF. The patients underwent continuous, in-hospital electrocardiographic (ECG) monitoring for 2–4 days following the procedure. The first outpatient clinic visit was 3–4 weeks after the ablation procedure. Subsequent follow-up visits consisted of a clinical interview, ECGs, and/or 24 h Holter monitoring every 3 months for up to 12 months after the last procedure, then every 6–12 months at our cardiology clinic if no recurrent arrhythmia was identified. Patients with any arrhythmic or ambiguous symptoms were encouraged to use a patient-activated event recorder for 30 consecutive days. For the detection of any asymptomatic events, we used an auto-triggered external loop recorder for 14 consecutive days. Recurrence was defined if an arrhythmia lasting longer than 30 s was documented after the 3-month blanking period in accordance with the latest guidelines [8].

Endpoint of the study

Long-term AF freedom was the primary endpoint for this study. Secondary endpoints included all-cause mortality, stroke, and HF-related unplanned hospitalizations during the post-ablation follow-up (defined as the composite endpoint). Planned readmissions, including hospitalizations for repeat ablation procedures, were not counted as outcomes in this measure.

Statistical analysis

Continuous data are expressed as the mean $\pm$ standard deviation for normally distributed variables or as the median [25th, 75th percentiles] for non-normally distributed variables, and they were compared using a Student t test or Mann–Whitney U test, respectively. Categorical variables were compared with the chi-square test. A Kaplan–Meier analysis was used to determine the percentage of patients free from AF recurrence, HF-related hospitalizations, and the composite endpoint after the procedure. A Cox method was used to determine the predictors of LV reverse remodeling, and variables whose univariate analyses had a p-value $<$ 0.1 were included. A probability value of $p < 0.05$ indicated statistical significance.

Results

Patient characteristics

A total of 106 patients consisting of 51 (48.1%) patients with HFrEF and 55 (51.9%) with HFpEF were included in the study. The patient clinical characteristics are summarized in Table 1. HFpEF patients more likely had paroxysmal AF, a higher LVEF, a smaller LV diastolic diameter (LVDd), and a lower N-terminal pro brain natriuretic peptide value. Among them, 11 (21.6%) HFrEF and 15 (27.3%) HFpEF patients had a history of a hospitalization due to HF prior to the procedure.

All patients underwent successful PVAI during the initial procedure. The mean number of procedures was 1.4 $\pm$ 0.5. Substrate modification was added in 22 (43.1%) HFrEF and 16 (29.1%) HFpEF patients. Procedural complications were observed in 1 (1.9%) HFrEF and 3 (5.5%) HFpEF patients, respectively. Cardiac tamponade requiring pericardiocentesis, transient air embolism in the right coronary artery, and asymptomatic right phrenic nerve injury were observed in 2, 1, and 1 patients, respectively, however, all recovered with conservative treatment. At the final follow-up, low-dose AADs were prescribed in 17 (33.3%) HFrEF and 12 (21.8%) HFpEF patients (Table 2). Follow-up echocardiography was performed at a mean of 13.2 $\pm$ 10.9 months after the initial procedure.

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