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Original article

Persistent left atrial remodeling after catheter ablation for non-paroxysmal atrial fibrillation is associated with very late recurrence

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ABSTRACT

Background: This study aimed to evaluate the association between left atrial (LA) structural remodeling and very late recurrence [VLR; initial recurrence >12 months after catheter ablation (CA)] after successful CA for non-paroxysmal atrial fibrillation (AF).
Methods: We retrospectively evaluated 63 patients who underwent initial, single ablation for drug-refractory persistent or long-standing persistent AF and those who had no recurrence in the first year after CA. We followed patients for a mean of 3.2 ± 1.5 years and divided them into VLR and no-recurrence (NR) groups. Before and 3 months after ablation, all patients were subjected to 64-slice multidetector computed tomography scanning to estimate LA volume, including maximum and minimum volume during the cardiac cycle (LAMaxV and LAMinV, respectively), and the LA emptying fraction.
Results: VLR occurred in 21 patients. The reduction rate of LAMaxV after CA was significantly larger in the NR group than in the VLR group (25 ± 19% vs. 5 ± 18%, $p = 0.0002$). Receiver operating characteristic analysis was performed to determine the best cut-off values in the prediction of VLR. The highest area-under curve was obtained with post-CA LAMinV [0.828 (95% confidence interval, 0.712–0.912), $p < 0.0001$], with a best cut-off value of 44 mL (sensitivity 81.0%, specificity 81.0%).
Conclusions: Persistent LA structural remodeling after initially successful CA for non-paroxysmal AF may be an important risk factor for VLR.

Introduction

Radiofrequency catheter ablation (RFCA) is reportedly more efficacious than drug therapy in restoring sinus rhythm in patients with atrial fibrillation (AF) [1–3]. However, despite advances in ablation techniques, AF recurrence is common and a significant number of patients require repeat procedures. AF recurrence is divided into three types: early recurrence (ER: AF recurrence during the first 3 months after initial RFCA, i.e. the blanking period), late recurrence (LR: AF recurrence 3–12 months after initial RFCA), and very late recurrence (VLR: AF recurrence >1 year after initial RFCA). LR is mainly caused by electrical pulmonary vein (PV) reconnection [4,5]; on the other hand, we previously reported that VLR might be caused by the progression of AF substrates and generation of non-PV triggers [6,7].

The progression of structural remodeling is easily identified as left atrial (LA) enlargement, which is the surrogate marker for AF substrates. Because LA reverse remodeling can occur during short-term follow-up after sinus conversion by RFCA [8–14], it is possible that patients without sufficient reverse remodeling after

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successful RFCA have residual LA substrate, which might cause subsequent VLR.

This study aimed to evaluate the association between post-RFCA reverse remodeling and VLR during long-term follow-up after successful RFCA for non-paroxysmal AF.

Methods

Study design

The study design was a retrospective, single-center, case–control study. A pre-study power analysis indicated that a sample size of 56 patients was necessary as described below. A total of 293 patients with drug-refractory non-paroxysmal AF underwent initial, single RFCA at Sakurabashi-Watanabe Hospital between 2006 and 2010. Among these patients, 114 patients were still under follow-up in January 2014. In this patient population, we enrolled 42 and 21 patients with sufficient data set who experienced no recurrence (NR) and VLR, respectively. The other 51 patients include ER patients, LR patients, or NR and VLR patients with insufficient data set. Patients with ER and LR were not evaluated in this study. Final follow-up was performed in January 2014. Written informed consent for the ablation was obtained from all patients. The study protocol was approved by the institution's ethic committee.

Before the ablation procedure and after 3 months of follow-up, multidetector computed tomography (MDCT) was performed to assess LA reverse remodeling. Before the procedure, MDCT was performed during AF rhythm for all patients, and we assessed the LA maximum and minimum volume (pre-LAMaxV and pre-LAMinV, respectively) and LA emptying fraction [pre-LAEF; defined as (LAMaxV − LAMinV)/LAMaxV × 100]. Three months after RFCA, the same parameters were reassessed during sinus rhythm (post-LAMaxV, post-LAMinV, and post-LAEF). We retrospectively evaluated the association between these LA functional parameters and VLR.

Clinical variables

We analyzed the following clinical variables: age, gender, height, weight, body mass index (BMI), patient history [long-standing persistent AF (duration of non-paroxysmal AF), hypertension, diabetes mellitus, dyslipidemia, and obesity (defined as BMI $\geq$25 kg/m^2)], CHADS$_2$ score (C, congestive heart failure; H, hypertension; A, age $\geq$75 years; D, diabetes mellitus; and S, stroke), laboratory data [high sensitive C-reactive protein (hsCRP), estimated glomerular filtration rate, brain natriuretic peptide (BNP)], transthoracic echocardiography data (left ventricular diastolic and systolic dimensions, LA diameter, left ventricular ejection fraction, and mitral annulus velocity), computed tomography data (LAMaxV, LAMinV, and LAEF), and follow-up period. AF was categorized into three types: paroxysmal (AF terminated spontaneously within 7 days), persistent (AF episodes for more than 7 days or AF requiring termination by cardioversion), and longstanding persistent (AF lasting for more than 1 year). Both persistent AF and longstanding persistent AF were defined as non-paroxysmal AF; only these were evaluated in the present study.

Scan protocol and data acquisition of MDCT

MDCT was performed within 1 week before and 3 months after ablation. A 64-slice MDCT scanner (Brilliance CT 64, Philips Medical Systems, Cleveland, OH, USA) was used with the following parameters: collimation, 64 × 0.625 mm; gantry rotation time, 420 ms; effective tube current, 800–1200 mA (higher values in obese patients); and tube voltage, 120 kV. The scan technique was defined by the attending physician in charge. A bolus of nonionic iodinated contrast (Iopamirone 370, Bayer, Osaka, Japan) was injected through an antecubital vein at a flow rate of 0.67 mL/min/kg for 15 s, followed by a saline bolus flush. The scan was initiated according to the bolus-tracking method [6 s after the threshold of 120 Hounsfield units in the descending aorta]. Cardiac images from the carina to the apex of the heart were acquired during one breath-hold.

Using the Comprehensive Cardiac Analysis software on Extended Brilliance Workspace (ver. 4.5.5.5; 1035 Philips Medical Systems), LAMaxV and LAMinV in one cardiac cycle were automatically measured using a volumetric segmentation method (the contour detection was visually checked and manually corrected if considered necessary), and LAEF was calculated as mentioned earlier.

Electrophysiological study and RFCA

A 6-French (Fr) decapolar catheter was placed in the coronary sinus via the median antebrachial vein, while a 7-Fr decapolar catheter was placed in the superior vena cava and right atrium via the femoral vein. Three long sheaths were introduced into the left atrium using a single transseptal puncture technique. An initial intravenous bolus of heparin (150 IU/kg) was followed by continuous infusion to maintain an activated clotting time of >300 s. Pulmonary angiography was performed by injecting a contrast medium through the transseptal long sheaths into the left atrium. Electrical cardioversion was performed in all cases.

PV isolation was guided by either fluoroscopy or three-dimensional mapping. We used an ablation catheter with an 8-mm tip (Fantasista, Japan Lifeline Co., Ltd., Tokyo, Japan) before December 2009 and an irrigated ablation catheter with a 3.5 mm tip (Navistar THERMOCOOL, Biosense Webster, Diamond Bar, CA, USA) after January 2010 for mapping and ablation. All patients underwent extensive PV isolation using the double lasso technique. Radiofrequency energy was delivered for 30 s at each point: up to 30 W, with a temperature limit of 43 °C, or up to 35 W, with a temperature limit of 50 °C, when using an irrigated or non-irrigated catheter, respectively. CA was performed using a conventional electrophysiological and anatomical approach. Circumferential PV isolation (defined as abolition or dissociation of PV potentials) was successfully performed in all patients. We also attempted to ablate non-PV premature atrial contractions if they triggered AF or appeared frequently, and targeted atrial flutter coexisting with atrial tachycardia. If it was difficult to maintain sinus rhythm, we performed isolation of the superior vena cava, linear ablation of the cavotricuspid isthmus, left atrium roof, left atrium bottom, mitral valve isthmus, and complex fractionated atrial electrogram.

Patient follow-up

All patients were hospitalized with continuous rhythm monitoring for 3 days after the ablation procedure. Prescription of anti-arrhythmic drugs (AADs) at discharge and in the outpatient clinic was determined by the patient's attending physician as necessary. We directed patients to check their pulse rate and rhythm 3 times a day and to visit the outpatient clinic if they experienced a relapse of AF. All patients were scheduled for visits to the outpatient clinic at 1, 2, 3, 6, 9, and 12 months after ablation and every 6 months thereafter. An electrocardiogram was obtained at each visit. Holter electrocardiogram, transthoracic echocardiography, and MDCT were performed 3 months after ablation. Recurrence of AF/atrial tachycardia was defined as recurrent symptoms and/or documented AF/atrial tachycardia on electrocardiogram. A 3-month blanking period after ablation was employed. Recurrence type was categorized as mentioned earlier.