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Original article

Impaired renal function is associated with recurrence after cryoballoon catheter ablation for paroxysmal atrial fibrillation: A potential effect of non-pulmonary vein foci

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ABSTRACT

Background: Atrial fibrillation (AF) and chronic kidney disease (CKD) are closely related. The present study aimed to evaluate the association between estimated glomerular filtration rate (eGFR) and outcomes after cryoballoon catheter ablation for AF.
Methods: We included a total of 110 patients (64.0 ± 10.1 years, 64% men) with paroxysmal AF who underwent second-generation cryoballoon catheter ablation in this study. Recurrence and change in renal function after ablation were assessed by stratification of eGFR sub-groups.
Results: During a mean follow-up period of 9 months, 20 (18%) patients had AF recurrence after the first catheter ablation procedure. Multivariate Cox regression analysis showed that eGFR [hazard ratio (HR) 0.97, 95% confidence interval (CI) 0.93–0.99, $p = 0.047$], non-pulmonary vein (PV) ectopic beats at initial ablation (HR 2.92, 95% CI 1.03–8.27, $p = 0.043$), and history of stroke (HR 7.47, 95% CI 2.30–24.2, $p = 0.001$) were independent predictors of recurrence after the ablation. Among the CKD groups, recurrence was found in 7% (1/15), 12% (9/73), and 46% (10/22) of the eGFR ≥90 mL/min/1.73 m^2, eGFR 60–89.9 mL/min/1.73 m^2, and eGFR 30–59.9 mL/min/1.73 m^2 groups, respectively ($p = 0.001$). Kaplan–Meier survival curves demonstrated that patients with eGFR 30–59.9 mL/min/1.73 m^2 had significantly worse prognosis than did the other groups (log-rank $p < 0.001$). In addition, non-PV ectopic beats at initial ablation were detected in 7% (1/15), 14% (10/73), and 50% (11/22) of the patients among the three CKD groups, respectively ($p < 0.001$). No patients developed contrast-induced nephropathy after the catheter ablation procedure.
Conclusions: Low eGFR at baseline was an independent predictor of recurrence after cryoballoon ablation for paroxysmal AF. The presence of non-PV ectopic beats was significantly increased in patients with impaired renal function, which might be associated with a poor outcome.

Introduction

Atrial fibrillation (AF) is one of the major cardiovascular diseases, and its prognosis and morbidity are closely related with chronic kidney disease (CKD) [1,2]. The prevalence of AF in the general population and recurrence after cardioversion of AF were reported to be significantly increased in patients with impaired renal function [3,4]. With respect to the therapeutic approach to AF, recent studies evaluated the association between CKD and outcome in patients with AF who underwent radiofrequency catheter ablation, and found that impaired renal function was an independent predictor of AF recurrence after ablation [5–8]. The potential association of atrial remodeling may explain poor prognosis after the therapeutic approach to AF in CKD patients;

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however, the exact mechanism of poor outcome after AF ablation is unclear.

Cryoballoon catheter ablation of AF was recently developed to treat AF as an alternative to classical radiofrequency catheter ablation. Although these two procedures have similar success rates and prognoses, the cryoballoon ablation procedure requires a higher amount of contrast medium than does the radiofrequency catheter ablation, which appears to more severely affect post-procedural renal function [9,10]. Moreover, despite its low prevalence, development of contrast-induced nephropathy (CIN) is a major concern following cardiac catheterization procedure, especially among CKD patients [11]. To date, few reports have systematically assessed the relationship between renal function and outcome of catheter ablation of AF in patients who receive cryoballoon-based ablation procedure of AF.

Therefore, the present study was conducted to examine the association between renal function and prognosis after the cryoballoon ablation of AF. In addition, we also evaluated the changes in renal function and prevalence of CIN development during the catheter ablation procedure.

Methods

Study population

The study population was recruited retrospectively from a catheter ablation database at Nagoya University Hospital, Japan. This ablation database was approved by our institutional ethics committee. Patients who had undergone second-generation cryoballoon catheter ablation for paroxysmal AF for the first time between July 2014 and August 2015 were included in the study. The indications for catheter ablation for AF complied with the latest guidelines [12,13]. In brief, patients with symptomatic paroxysmal AF, who are refractory to antiarrhythmic and rate-control drugs or could not be given these drugs because of side effects or comorbidities, and patients who wished to receive catheter ablation therapy for AF despite the effectiveness of drug therapy, were referred for AF ablation. The exclusion criteria were as follows: (i) lost to follow-up within 3 months after catheter ablation; (ii) a history of a MAZE procedure; (iii) development of a major complication resulting in discontinuation of the ablation procedure; and (iv) left ventricular ejection fraction (LVEF) $< 40\%$ at baseline. Prior to the procedure, informed consent was obtained from all patients, in accordance with our hospital guidelines.

Examination course

Patients who were scheduled for catheter ablation treatment were admitted one day before the procedure. At admission, baseline blood testing, echocardiography, electrocardiography, and the Holter examination were performed. Antiarrhythmic agents, except for amiodarone and bepridil, were stopped five half-lives before ablation [14]. Transesophageal echocardiography was performed in all patients to confirm the absence of atrial thrombus. All patients underwent 3-dimensional computed tomography (320-row detector, dynamic volume computed tomography (CT) scanner; Aquilion ONE^{TM}, TSX-301C, Toshiba Medical Systems, Tokyo, Japan) for visualization of the left atrium and pulmonary veins (PV). Anticoagulant drugs, including novel anticoagulant agents, were continued during the procedure, as previously reported from our institution [15].

Ablation procedure

For the cryoballoon ablation procedure, vascular access was obtained via the right femoral and left subclavian veins. After the administration of 80–100 IU/kg bolus of heparin, a transseptal puncture was performed using a RF needle (Baylis Medical, Inc., Montreal, QC, Canada) and an 8-French (Fr) sheath under intracardiac echocardiography monitoring. A 15Fr steerable sheath (Flexcath Advance, Medtronic, Minneapolis, MN, USA) was introduced into the left atrium. Following all PV venography during raid ventricular pacing, the second generation 28-mm cryoballoon system (Arctic Front Advance, Medtronic) was advanced and placed on the ostium of each PV using an inner circular mapping catheter (Achieve, Medtronic). After the confirmation of PV ostium occlusion with cryoballoon by using contrast medium, 180-s cycle freeze ablation was repeated until electronic isolation of PV was achieved using the mapping catheter. During the freeze ablation of the right PV, pacing phrenic nerve stimulation was performed with a compound motor action potential monitoring in order to avoid phrenic nerve injury [16]. Finally, complete PV electronical isolation was confirmed by circular mapping catheter (Baylis Medical, Inc.). An 8-mm tip cryocatheter (Freezor MAX, Medtronic) was also available for additional touch-up freeze applications. After confirmation of complete PV isolation, we evaluated non-PV ectopic beats and AF occurrence with intravenous isoproterenol infusion, if needed. If an immediate AF recurrence initiated by non-PV ectopic beats or atrial flutter occurred, additional ablation of the non-PV foci and linear ablation were performed. All procedures were performed by a 3-dimensional electroanatomical mapping system (Ensite, NavX^{TM}, St. Jude Medical, Inc., St Paul, MN, USA). During the procedure, additional heparin was administered to maintain an activated clotting time of 300–350 s. After the procedure, total of intravenous saline infusion with more than 1000 mL continued until the day after ablation.

Classification of CKD

Classification of CKD stage was determined using the estimated glomerular filtration rate (eGFR) calculation at the baseline. The eGFR was calculated on the basis of the Japanese coefficient-modified Modification of Diet in Renal disease study equation: eGFR (mL/min/1.73 m^2) = $194 \times$ [serum Creatinine (mg/dL)]$^{-1.094} \times$ [age (years)]$^{-0.287} \times$ (0.739 if female) [17].

The study population was divided into three subgroups: patients with eGFR $\geq$90 mL/min/1.73 m^2 (CKD stage 1), patients with eGFR between 60 and 89.9 mL/min/1.73 m^2 (CKD stage 2), and patients with eGFR between 30 and 59.9 mL/min/1.73 m^2 (CKD stage 3). Patients with eGFR $<$30 mL/min/1.73 m^2 were not included in this study, because only one patient receiving chronic hemodialysis underwent cryoballoon ablation of AF during the study period. Serum creatinine levels were collected, and eGFR was calculated at baseline, 3 days, and 1 month after the procedure.

Follow-up

Patients remained hospitalized under continuous rhythm monitoring for 3 days after the procedure. After discharge, patients were followed-up through the outpatient clinic both in our hospital and by a nearby practitioner at minimum every month after ablation. At the time of each follow-up visit, patients underwent 12-lead electrocardiography, and were questioned about any symptoms related to the presence of arrhythmia. If patients were suspected of having had an emergent arrhythmia, but had no evidence of arrhythmia at the time of examination, additional Holter monitoring and short duration follow-up were performed. Twenty-four hour–Holter monitoring was performed in all patients at 1 month after ablation. If patients had an episode of AF, antiarrhythmic drugs that had been discontinued before the procedure were re-administered. AF or atrial tachycardia occurring

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