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Transformation from persistent atrial fibrillation to paroxysmal type after initial ablation predicts success of repeated ablation

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ABSTRACT

Background: If transformation from persistent atrial fibrillation (AF) to paroxysmal AF after catheter ablation had impacts on the outcome of repeated ablation was unclear. This study aimed to explore whether the type of recurrent AF after ablation for persistent AF was associated with recurrence after repeated ablation.
Methods and results: This was a retrospective cohort study. 116 persistent AF patients undergoing the second ablation due to a failed initial ablation were enrolled in our study. Patients with recurrent paroxysmal AF after initial ablation were categorized as Group A (47 patients) while those with recurrent persistent AF were categorized as Group B (69 patients). The study endpoint was defined as any episode of AF, atrial tachyarrhythmia or atrial flutter lasting for >30 s, after the 3 month blanking period following repeated procedure. After 3–72 months (median: 24 months) of follow-up from repeated ablation, 54 (47%) patients suffered from recurrence after repeated ablation. In univariate analyses, Group B suffered a higher risk for recurrence than those in Group A (hazard ratio: 2.05, 95% confidence interval: 1.14–3.70, $P = 0.01$). Besides recurrent AF type, larger left atrial dimension at repeated procedure and pulmonary vein reconnection also predicted success of repeated ablation. In multivariate analysis, patients in Group B still had a 1.91-fold higher risk for recurrence than those in Group A (HR: 1.91, 95% CI: 1.06–3.44, $P = 0.03$).
Conclusions: After persistent AF ablation, transformation from persistent AF to paroxysmal AF is independently associated with success of repeat ablation.

1. Introduction

Atrial fibrillation (AF) is the most common atrial arrhythmia and associated with increased mortality and morbidity. Catheter ablation of AF is effective in restoring and maintaining sinus rhythm (SR), especially for paroxysmal AF. Nevertheless, the success rate of catheter ablation for persistent AF is unsatisfied with about 50% of patients suffering from recurrence in the first year following the procedure [1]. Therefore, regarding persistent AF, repeated ablation is usually needed in clinical practice.

How to predict the outcome after repeated ablation is helpful for clinicians to make an individual treatment plan and avoid overtreatment. Left atrial enlargement, renal function, original AF type and recurrence with AT were reported to be associated with the outcome of repeated ablation [2–5]. However, few studies evaluated the value of recurrent AF type after initial ablation of persistent AF in predicting the outcome after repeated ablation. Persistent AF might transform to paroxysmal AF after ablation. Transformation from persistent AF to paroxysmal AF not only indicates that initial ablation might partly modify the substrates maintaining AF but also contributes to atrial reverse remodeling [6–8]. Therefore, we speculated that after initial ablation of persistent AF, transformation from persistent AF to paroxysmal AF might be associated with a good outcome after repeated ablation.

2. Methods

2.1. Study population

The present study was a retrospective cohort study. We enrolled consecutive patients from January 2011 to October 2016 at Shaoxing People's Hospital (Shaoxing Hospital of Zhejiang University) and Sir Run Run Shaw Hospital with follow-up ending in October 2017. Inclusion criteria were as follows: 1) receiving the first time ablation of persistent AF at our centers; 2) suffering from AF recurrence after the first time ablation, after the 3 month blanking period; and 3) undergoing repeated ablation at our centers according to current guidelines [1]. Exclusion criteria included: 1) recurrent atrial arrhythmias

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involving atrial tachyarrhythmia (AT) or atrial flutter (AFL); 2) reversible causes for AF; 3) incomplete medical records; 4) severe heart disease (ejection fraction <35%, a prosthetic heart valve, moderate or severe valvular heart diseases according to AHA guidelines [9], dilated cardiomyopathy, hypertrophic cardiomyopathy); and 5) life expectancy <1 year. Enrolled patients were divided into two groups according to the type of recurrent AF after initial ablation. Patients with recurrent paroxysmal AF were categorized as Group A while those with recurrent persistent AF were categorized as Group B. All patients provided written informed consent, and the study was conducted in accordance with the declaration of Helsinki. The Ethics Committee of Shaoxing People's Hospital (Shaoxing Hospital of Zhejiang University) and Sir Run Run Shaw Hospital approved the study design.

The type of AF in our study was classified according to 2016 ESC AF guideline [1]. Paroxysmal AF was defined as AF that terminated spontaneously or under interventions within 7 days of onset. Persistent AF was defined as AF that lasted >7 days. The type of recurrent AF was identified according to the initial recurrence after the 3 month blanking period following initial ablation.

2.2. The initial ablation procedure

Antiarrhythmic drugs (AADs) were discontinued >5 half-lives before ablation, except for amiodarone, which was discontinued >2 weeks before ablation. All patients received antral pulmonary vein isolation (PVI) guided by three-dimensional left atrium (LA) mapping that had been described in detail in our previous study [10]. Briefly, two trans-septal sheaths were introduced into LA. Geometry of LA and pulmonary veins (PVs) was reconstructed using the EnSite Velocity 3.0 system. Continuous radiofrequency ablation was performed to encircle the ipsilateral PVs (target temperature: 45°, maximum power: 35 W, infusion rate: 17 ml/min). Linear ablation (LA anterior line, LA roof line, and mitral isthmus line) and/or complex fractionated atrial electrogram (CFAE) ablation were performed at the operators' discretion. If AFL was documented before or during the procedure, cavotricuspid isthmus (CTI) ablation was performed. Procedural endpoint was bidirectional conduction block of all PVs and linear lesions (if created). If SR was not achieved after all the above ablation processes, cardioversion was conducted to restore SR.

2.3. The repeat ablation procedure

During redo-ablation, initially, incomplete PVI was assessed by a circular mapping catheter and linear lesions (if created) were checked based on differential pacing. If reconnected PV potentials and linear lesion conduction were identified, enforcing previous ablation sites was performed. If linear ablation was not performed during initial procedure, linear lesions were added as the standard lesion set. Additional ablation including empirical superior vena cava isolation and/or CFAE ablation, was performed at the operators' discretion. The endpoints of repeated procedure were complete PVI and bidirectional linear block. If AF continued after all the above ablation processes, cardioversion was conducted to restore SR.

2.4. Post-ablation management and follow-up

In our centers, no matter initial or repeated ablation, if there were no contraindications or intolerance, all patients received oral amiodarone (100–200 mg daily) for 3 months following the procedure. Thereafter, amiodarone was used at the physicians' discretion. Anticoagulants were continued for at least 3 months following the procedure, and thereafter were used according to the risk of thromboembolism events.

After repeated ablation, patients were followed in the outpatient clinic regularly at 1, 3, 6, and 12 months and every 6 months thereafter. Additional follow-up visits were encouraged whenever arrhythmia-related symptoms occurred. Follow-up visit included intensive questioning for arrhythmia-related symptoms, ECG and 24 h Holter recording. If patients were implanted with devices that could record heart rhythm, recordings were evaluated during every visit.

The study endpoint was defined as any episode of AF, AT or AFL (confirmed by ECG or Holter recordings or implanted devices) lasting for >30 s, after the 3 month blanking period following repeated procedure.

2.5. Statistics

Normal distribution data were presented as mean ± standard deviation and were compared using Student's *t*-test. Skewed data were summarized as median (minimum, maximum). A Mann–Whitney test was performed to compare skewed data between groups. Categorical data were expressed as counts and were compared using Pearson's χ^2 test. A Kaplan–Meier analysis with a log-rank test was used to compare survival curves between groups. Univariate Cox analyses were performed to evaluated predictive value of clinical variables on endpoint events. Multivariate Cox proportional-hazards regression with forward likelihood ratio was performed to identify independent risk factors for endpoint events. All potential confounders based on known clinical relevance and parameters that had a *P*-value <0.20 in univariate Cox analyses were entered into the model. Considering the potential effect of amiodarone on the type of recurrent AF after initial ablation, we performed an additional analysis after excluding patients who were on amiodarone when recurrent AF after initial ablation was identified. All data were analyzed using SPSS 20.0. A *P* value <0.05 was considered to be statistically significant.

3. Results

3.1. Study subjects and characteristics of patients

A total of 706 patients underwent the first time catheter ablation of persistent AF at our centers from January 2011 to October 2016. Among these patients, 203 patients received repeated ablation at our centers. 87 cases were excluded and 116 patients were included in our cohort (82 patients suffering recurrent arrhythmia involving AT and or AFL; 3 patients withdrawing consent; 2 patients missing data). Among enrolled patients, 47 patients suffered from recurrence with paroxysmal AF (Group A), and the remaining 69 patients suffered from recurrent persistent AF (Group B). A total of 30/116 (26%) patients were on amiodarone when recurrent AF after initial ablation was identified (17/69 in Group A vs 13/47 in Group B, $P = 0.72$). In Group A, 21/47 (45%) patients converted spontaneously and the others converted under interventions (pharmacological cardioversion and/or direct current cardioversion). The clinical characteristics of patients are summarized in Table 1. In spite of no statistical significance, there was a trend toward a smaller LA in Group A. There was no difference in the remaining baseline clinical characteristics between the two groups. The follow-up duration of enrolled patients was 3–72 months (median: 24 months). During the follow-up period, 6/47 (13%) and 7/69 (10%) patients were lost in Groups A and B, respectively. The reasons for missing were as follows: 5 patients refused follow-up (2 in Group A, 3 in Group B); 1 patient was dead due to an accident (Group A); 1 patient was dead due to gastric cancer (Group B); 4 patients were lost due to population mobility (2 in Group A, 2 in Group B) and 2 patients were lost due to other reasons (1 in Group A, 1 in Group B). Baseline characteristics of these patients were similar to those finishing follow-up (Supplementary table1).

During initial ablation, 106/116 (91%) and 29/116 (25%) patients received linear ablation and CFAE ablation, respectively. And 19/116 (16%) patients received both ablation strategies. PV reconnection was found in 89/116 (77%) patients. PV reconnection was more frequently identified in Group A (87% vs 70%, $P = 0.03$). Among patients receiving linear ablation at index ablation, reconnection within linear lesions was identified in 75/106 (71%) patients. Reconnection along LA anterior line, LA roof line, and mitral isthmus line was found in 70/106 (66%), 66/106 (62%) and 64/106 (60%) patients, respectively. Additional ablation was performed in 37/116 (32%) patients. No difference in procedural characteristics was found between the two groups. The procedural characteristics are shown in Table 1.

3.2. Recurrence free survival and predictors of recurrence

After the follow-up period, 54 (47%) patients suffered from recurrence after repeated ablation. Recurrence rate was significantly lower in Group A (16/47 vs 38/69, $P = 0.03$). In patients suffering recurrence after repeated ablation, recurrent AF type after initial ablation was more likely to be persistent (70% vs 50%, $P = 0.03$), left atrial dimension at repeated procedure was larger (46.8 ± 3.9 vs 44.8 ± 4.2, $P = 0.01$) and the rate of PV reconnection was lower (67% vs 85%, $P = 0.02$). What's more, in spite of no statistical significance, patients with recurrence trended to be male gender (79% vs 65%, $P = 0.09$), and have a lower estimated glomerular filtration rate (eGFR) (88 ± 16 vs 93 ± 17 ml/min, $P = 0.11$). No difference in other characteristics was detected between patients with and without recurrence after repeated ablation.

In univariate Cox analyses, patients in Group B suffered a higher risk for recurrence than those in Group A (HR: 2.05, 95% CI: 1.14–3.70, $P = 0.01$). Besides the type of recurrent AF after initial ablation, the univariate predictors of recurrence after repeated ablation included left atrial dimension at the second procedure ($P = 0.02$) and PV reconnection identified during repeated ablation ($P = 0.03$). After adjusting for age, sex, duration of AF, eGFR, hypertension, diabetes, coronary heart disease, left ventricular ejection fraction, use of amiodarone, additional ablation and procedure time during the second ablation, patients in