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Characteristics and long-term catheter ablation outcome in long-standing persistent atrial fibrillation patients with non-pulmonary vein triggers

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ABSTRACT

Background: There are limited literatures regarding the non-pulmonary vein (NPV) triggers in long-standing persistent atrial fibrillation (LSPAF). The goal of the present study was to investigate the characteristics and long-term outcome of catheter ablation among these patients.
Methods: The study included 776 patients (age 53.59 ± 11.38 years-old, 556 males) who received catheter ablation for drug-refractory atrial fibrillation (AF). We divided these patients into 3 groups. Group 1 consisted of 579 patients with paroxysmal AF (PAF), group 2 consisted of 103 patients with persistent AF (PerAF) and group 3 consisted of 94 patients with long-standing persistent AF (LSPAF). The average follow-up duration was 28.53 ± 23.21 months.
Results: The clinical endpoint was the recurrence of atrial tachyarrhythmia. Among these 3 groups, higher percentages of male (93.6%, $P < 0.001$), NPV triggers (44.7%, $P < 0.001$), longer AF duration (6.65 ± 6.72 years, $P = 0.029$), larger left atrium diameter (44.44 ± 6.79 mm, $P < 0.001$), and longer procedure time (181.94 ± 70.02 min, $P < 0.001$) were noted in LSPAF. After the first catheter ablation, the recurrence rate of AF was highest in LSPAF (Log Rank, $P < 0.001$). Larger left atrium diameters (LAD) ($P = 0.006$; HR: 1.063; CI: 1.018–1.111) and NPV triggers ($P = 0.035$; HR: 1.707; 1.037–2.809) independently predicted AF recurrence in LSPAF.
Conclusions: Compared with PAF and PerAF, LSPAF had a higher incidence of NPV triggers and worse long-term outcome after catheter ablation. NPV triggers and LAD independently predicted AF recurrence after catheter ablation in LSPAF.

1. Background

Atrial fibrillation (AF) is the most common cardiac arrhythmia in the clinical practice and is also a major risk factor for ischemic stroke. The pulmonary vein (PV) triggers were recognized as important sources of ectopic beats to initiate paroxysmal AF (PAF) [1] and PV isolation has been a cornerstone treatment strategy to cure PAF because of its superior benefits in maintenance of sinus rhythm and improvement of clinical symptoms showed in a prior study [2] and was recommended by the European Society of Cardiology (ESC) AF guidline [3] and the 2014 American College of Cardiology/American Heart Association (ACC/AHA/HRS) AF guideline [4]. However, AF recurrences after PV isolation in persistent AF (PerAF) and long-standing persistent AF (LSPAF) were higher than PAF and the optimal strategy of catheter ablation in PerAF and LSPAF remains uncertain [5,6]. Several investigators reported the presentation of non-pulmonary vein (NPV) triggers and its clinical importance in PAF [7], but there are limited literatures about NPV triggers in the patients with LSPAF. The present study aimed to analyze the characteristics, incidence and distribution of NPV triggers in the patients with AF receiving catheter ablation, especially LSPAF patient population.

2. Methods

2.1. Study population

The present study enrolled 776 consecutive patients who underwent catheter ablation of drug-refractory, symptomatic AF between 2003 and 2011 in Taipei Veteran General Hospital (VGH). Among these patients, 94 patients (12%) were diagnosed as LSPAF. All the patients underwent the routine protocol to identify PV or NPV trigger foci. The mean

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follow-up duration of AF was 28.53 ± 23.21 months. Classification of AF type was based on AHA/ACC/ESC guidelines [3,4], in which PAF was defined as self-terminated AF in 7 days or less, PerAF was defined as incessant AF lasting >7 days and <12 months, and LSPAF was defined as continuous AF for >1 year. The study was approved by the VGH institutional review board (IRB).

2.2. Electrophysiological study and mapping strategy

The details of the procedure protocol were described in our previous studies [7–13]. In brief, all the patients stopped taking antiarrhythmic agents except amiodarone for >5 half-lives before the procedure and each of them underwent electrophysiological study and catheter ablation under the fasting and non-sedated state. We placed a 7-French deflectable decapolar polar catheter with a 2-mm interelectrode distance and 5-mm space between each electrode pair (St. Jude Medical, Minnetonka, MN, USA) into the coronary sinus (CS) through the internal jugular vein access. A decapolar circular catheter (Spiral-SC, St. Jude Medical, Minnetonka, MN, USA) was placed into left atrium via femoral venous access after atrial trans-septal puncture. Biatrial electroanatomic geometries and sequential contact voltage maps were constructed in the patients using a NavX system (St. Jude Medical, Minnetonka, MN, USA). If patients presented to the laboratory in sinus rhythm initially, a designed algorithm to facilitate the initiation of AF was used to find the spontaneous onsets of atrial ectopic beats or repeat short runs of sustained AF with or without isoproterenol infusion (4–8 μg/min). If atrial ectopy did not occur, intermittent burst pacing from right atrium, coronary sinus, and PV or administration of intravenous high-dose adenosine (18–24 mg) was performed. If AF still could not be induced, continuous burst pacing would be used until sustained AF was induced. The initiating site was considered as the earliest and most consistent atrial activation site induced AF. External cardioversion was performed to restore sinus rhythm and any spontaneous reinitiation of AF would be observed after cardioversion. AF would be induced at least twice in all the patients to ensure the reproducibility of AF induction by the methods above and to confirm the triggers of AF.

2.3. Radiofrequency catheter ablation in PVI and NPV triggers

The stepwise procedure of catheter ablation was achieved as described in our previous studies [10–12]. Patients received continuous circumferential lesions which created encircling the atrial side of bilateral PV antrum guided by the NavX system with a non-irrigated tip ablation catheter (Livewire TC, St. Jude Medical, St. Paul, MN, USA, before 2005) or irrigated tip ablation catheter (Chilli II, EPT, Boston Scientific Corporation, Natick, MA, USA or Cool Path, St. Jude Medical, St. Paul, MN, USA, after 2006). Radiofrequency energy was set to 25–35 W and 40 s for each lesion with temperature not >40 °C. Successful PV isolation was demonstrated by obtaining the entrance and exit blocks of the PVs, and absence of any electrical activity inside the PV or dissociated PV activity during AF. If AF persisted after isolation of PV, additional linear ablation was performed at both the anterior roof and lateral mitral isthmus. Cavotricuspid isthmus ablation was performed with an 8 mm-tip EPT ablation catheter (Boston Scientific Corporation) with a maximum power of 70 W and temperature of 70 °C. Bidirectional conduction block of linear ablation was confirmed after restoration to sinus rhythm. In patients with PerAF or LSPAF, if AF did not stop after isolation of PV and series of linear ablations, an additional complex fractionated atrial electrogram (CFAE) ablation was performed sequentially based on the results of the CFAE maps. The CFAE ablation was confined to the maximal CFAEs with fractionation interval (FI) <50 ms in the left and right atrium [13,14]. The endpoint of the CFAE ablation was to obtain a prolongation of the cycle length, elimination of the CFAEs with FI >120 ms or the local fractionated potential (bipolar voltage <0.05 mV). If the AF still did not stop after the above procedures, sinus rhythm was restored by external cardioversion.

The location of NPV foci was identified by evaluation of the activation sequence of the high right atrium (RA), His bundle area, and CS. A duodecapolar catheter (1-mm electrode length and 2-mm interelectrode spacing) was placed to superior vena cava (SVC) and atriocaval junction area to detect SVC triggers. A deflectable halo catheter with 10-mm paired spacing (Halo, Cordis-Biosense-Webter) was placed around the tricuspid annulus for mapping right atrial NPV triggers. The time interval (<0 ms) between the high RA and His bundle area during sinus rhythm and ectopy can differentiate the site of ectopy as the SVC, upper crista terminalis, or PV. Simultaneous mapping of the SVC and right PV was done to clarify the true initiating foci. If the earliest activation site was in the interatrial septum (IAS), simultaneous mapping of the right and left septum was performed. To map NPV trigger from left atrium (LA), the activation time interval between the proximal and distal pairs of the CS catheter during ectopy was evaluated. Ectopic beats form the ligament of Marshall (LOM) was identified according to the electrophysiological characteristics described in our previous report [15]. In patients with NPV triggers, catheter ablation toward the earliest electrical activity or a local unipolar QS pattern of the ectopic beat preceding the onset of AF was performed. The endpoint of NPV triggers ablation was disconnection between the SVC and RA, CS and RA, and elimination of other NPV ectopic beats with negative provocation of AF [12].

2.4. Post-ablation follow-up of AF recurrence and repeat procedures

After the ablation was done, antiarrhythmic medicines were prescribed for 4 to 8 weeks to prevent the early recurrence of AF. Patients received follow-up visits every 1 to 3 months at our cardiology out-patient clinic or the referring cardiologist clinic for more than one year, where routine electrocardiograms were obtained. The 24-h Holter monitoring or 1-week cardiac event recordings were arranged every 3 months in the first year after the ablation procedure and when the patients experienced symptoms suggestive of a tachycardia. After one year after procedure, the patients received regular follow-up visits ever half a year. Long-term efficacy was assessed according to resting surface 12-leads electrocardiograms, 24-h Holter monitoring and/or 1-week cardiac event recorder. The clinical endpoint was the recurrence of atrial tachyarrhythmia, which was defined as an episode lasting for >30 s after the ablation. The patients were suggested to receive a second ablation procedure, or antiarrhythmic medicines if more than one episode of recurrent symptomatic atrial tachyarrhythmia with a duration longer than 30 s to 1 min per episode was documented.

2.5. Statistical analysis

All continuous data were presented as the mean value and standard deviation for normally distributed continuous variables and proportions for categorical variables. Differences of continuous values between 2 groups were assessed using an unpaired two-tailed *t*-test for normally distributed variables. The One-Way ANOVA method was used to analyze the data among 3 groups. A Kaplan-Meier survival analysis with log rank was performed to demonstrate the AF recurrence. Differences between nominal variables were compared by the chi-squared test. A multivariable analysis was performed with the Cox stepwise forward regression model to determine the independent predictors of the AF recurrence. The variables selected in multivariable analysis model were those with a P value <0.1 in univariate analysis model. Confidence intervals were all calculated in the 95% interval. All statistical significances were set at a P value <0.05. The statistical analyses were conducted with SPSS Statistic 18.0 software (Chicago, IL, USA.)

3. Results

3.1. Baseline characteristics and AF characteristics of study patients

The present study included 776 patients (age 53.59 ± 11.38 years-old, 556 males) who underwent catheter ablation for symptomatic drug-refractory AF. These patients were divided to 3 groups. Group 1 consisted of 579 patients with PAF, group 2 consisted of 103 patients with PerAF and group 3 consisted of 94 patients with LSPAF. The baseline characteristics and echocardiographic parameters of the 3 groups are shown in Table 1. Patients in LSPAF were more likely to be male, higher body mass index (BMI), larger dimensions of the left atrium (LAD), and lower left ventricular ejection fraction (LVEF). The incidence of congestive heart failure in LSPAF was higher than other 2 groups. Table 2 shows the AF characteristics and procedure parameters. Patients in LSPAF had longer AF duration (6.65 ± 6.72 years, $P = 0.029$) and higher incidence of NPV triggers (44.7%, $P < 0.001$), compared to that in PAF and PerAF, respectively.

3.2. AF recurrence and NPV triggers

Fig. 1A shows the recurrence rate of all patients with AF, and 335 (43.2%) patients had recurrences after first ablation. The overall AF recurrence rate was 26.8% in the first year, 35.4% in the second years and 42.0% in the fifth years after the index procedure. The AF recurrence rate was 37.1% for PAF, 49.5% for PerAF and 73.4% for LSPAF during a mean follow-up period of 28.53 ± 23.21 months (Log Rank $P < 0.001$). We classified all patients into 2 groups by different ablation time periods (2003–2006 and 2007–2011) to examine the possible effect of improvement of catheter ablation technologies and techniques. Among overall AF patients, there were no significant difference between the 2 groups ($P = 0.099$). In PAF group, there was lower recurrent rate in those received ablation later ($P < 0.001$). However, in patients with PerAF and patients with LSPAF, there were no differences in AF recurrence ($P = 0.058$ and 0.603, respectively).

Kaplan–Meier analysis curves of all AF patients with NPV triggers and without NPV triggers are shown in Fig. 1B. Patients with NPV triggers had worse prognosis than those without NPV triggers in all 3 groups, respectively. Among patients without NPV triggers, those in LSPAF had a higher recurrence rate and the similar finding was also observed among patients with NPV triggers (Fig. 1C, D).

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