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Documentation of pulmonary vein isolation improves long term efficacy of persistent atrial fibrillation catheter ablation☆,☆☆

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ABSTRACT

Background: The aim of this study was to investigate the efficacy of catheter ablation in the treatment of persistent atrial fibrillation (AF) and the predictors of arrhythmia recurrence.
Methods: Absence of atrial tachyarrhythmia (AT) recurrence during a mid-term follow-up was correlated with several clinical and procedural characteristics in a population of 82 patients aged 20–70 years who had experienced at least one documented relapse of persistent AF during a single trial of antiarrhythmic drug therapy. Electrophysiological success of ablation was declared when all identified PVs were isolated (confirmation of entry and exit block). Patients were followed for a maximum of 24 months after the blanking period with outpatient visits, ECG recordings, 24-hour Holter monitoring, and weekly transtelephonic monitoring for 30 s.
Results: Electrophysiological success was documented in 38/82 (46.3%) patients. During a mean follow-up of 24.7 ± 4.2 months, 69/82 (84.1%) patients presented at least one episode of AT after the 2 month blanking period. According to univariate and multivariate logistic regression analyses, only an electrophysiologically successful ablation significantly correlated with the absence of documented AT relapse (OR 5.32, 95% CL 1.02–27.72; p = .0472).
Conclusions: Mid-term outcome of a single procedure of catheter ablation without the adjunction of antiarrhythmic drug therapy is poor in patients with persistent AF. Documented PV isolation is useful to increase the success rate of circumferential PV ablation even in persistent AF patients.

1. Introduction

According to the most recent HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation (AF) [1], ablation strategies which target pulmonary veins (PVs) or PV antra are the cornerstone for most AF ablation procedures, and if PVs are targeted, complete electrical isolation should be the goal. PV isolation has been an effective means of preventing tachyarrhythmia recurrences particularly when AF is paroxysmal, that is when triggers have a predominant role [2–7]. On the contrary, the role of PV isolation is still debated when AF is persistent or "long standing": not only is PV isolation not enough to treat these forms of AF [8,9], but also, according to some reports, PV isolation does not seem necessary to prevent AF recurrences [10–13].

Catheter Ablation for the Cure of AF (CACAF-2) Study was a prospective, randomized trial designed to compare the efficacy of radiofrequency catheter ablation with combined lesions in the right and left atria, in preventing AF recurrences among patients with recurrent, persistent AF refractory to 1 antiarrhythmic drug, in comparison to the best pharmacological therapy [14]. In this sub-study we investigated the role of

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several clinical and procedural parameters for predicting mid-term (up to 26 months) freedom from atrial tachyarrhythmia (AT), among population of CACAF-2 Study.

2. Methods

2.1. Patients

The enrollment criteria, rationale and power calculation for CACAF-2 Study have been previously reported [14]. In summary, patients between 20 and 70 years of age who had experienced at least one documented relapse of persistent AF during a single trial of antiarrhythmic drug were enrolled in the study. Each patient was randomized to catheter ablation (*Ablation group*) or antiarrhythmic drug therapy alone (*Control group*) in a 2:1 manner. In summary: 87 patients were randomized to the *Ablation group* and 42 patients to the *Control group*. Among patients randomized to the *Ablation group*, 82 underwent transcatheter ablation and represent the study population discussed in this manuscript (Fig. 1).

2.2. Catheter ablation

Patients had to be on oral anticoagulant therapy for at least 1 month before ablation. Left atrium and PVs were explored using a transseptal approach. Real-time 3D left atrial maps were reconstructed using a nonfluoroscopic navigation system (CARTO®, Biosense Webster Inc., Diamond Bar, California). Maps were acquired during AF or pacing from the coronary sinus. Radiofrequency pulses were delivered using a 3.5-mm NAVISTAR® THERMOCOOL® catheter (Biosense Webster Inc., Diamond Bar, California) with a temperature limitation of 45 °C and a radiofrequency energy up to 42 W. Radiofrequency energy was delivered up to 120 s until local electrogram amplitude was reduced by ≥80%. To reduce the risk of the catheter tip overheating, a fine back-and-forth movement of the catheter was recommended during radiofrequency delivery at the ablation site. The ablation lines consisted of contiguous focal lesions deployed at a distance ≥5 mm from the ostia of the PVs, creating a circumferential line around each PV. In addition, the left inferior PV was connected to the mitral annulus (mitral isthmus), and a left atrial roof line connecting the superior encirculations of the PVs' ostia was created. Demonstration of conduction block through the lines was not required.

PV isolation had to be checked at the end of anatomical circumferential ablation after spontaneous restoration of normal sinus rhythm or after electrical cardioversion. A circular decapolar mapping catheter (LASSO®, Biosense Webster Inc., Diamond Bar, California) was used to check PV isolation. Each PV ostium was considered completely isolated when: 1) PV potentials disappeared or were disconnected (entry block); and 2) pacing from at least 3 points inside the encircled PV with a stimulus of 10 mA of amplitude and 2 ms of duration allowed local capture without left atrium capture (exit block). PV isolation after circumferential ablation was not mandatory.

Patients with conduction along the cavo-tricuspid isthmus underwent inferior vena cava–tricuspid annulus isthmus ablation after completion of the left atrium ablation, in the same session.

2.3. Follow-up

A blanking period of 2 months was scheduled in order to allow the consolidation of radiofrequency lesions and resolution of any pericarditis secondary to the RFA. Before the end of the blanking period, one electrical cardioversion was allowed to restore sinus rhythm in the event of persistent AF, and one transcatheter ablation in the event of intolerable recurrent atrial flutter/tachycardia.

Patients were followed for a maximum of 24 months after the blanking period with outpatient visits and ECG recordings at 2, 5, 8, 11, 14, 17, 20, 23 and 26 months and 24-hour Holter monitor recordings at 2, 5, 8, 14, 20, and 26 months. In order to exclude asymptomatic AT recurrences, each patient was provided with a personal device that had the capability of recording a single-lead ECG during an event and also transmitting the recording to a monitoring center [15]. The transtelephonic monitoring (TTM) period started immediately after the blanking period, and continued for 24 months. The patients were asked to record a 30 second ECG once a week, and a 30 second ECG in the event of palpitation. Patients were also proactively followed by the monitoring center.

Transthoracic echocardiograms were performed at the first day post-procedure and at 5, 14, and 26 months to collect information regarding pericardial effusion, volume parameters, and valve abnormalities.

2.4. Definitions

Primary endpoint: total absence of any documented AT, including AF and atrial tachycardia/flutter, lasting >30 s during the first 24 months after the 2-month blanking period, in the absence of antiarrhythmic drugs, after a single ablation procedure.

Electrophysiological success: isolation of all identified PVs, with documentation of entry and exit block.

AF history: time since the first diagnosis of arrhythmias was detected.

3. Statistical methods

Continuous measurements were expressed as mean ± SD (range), and were compared by means of Student's *t*-test with equal or unequal variances. The normality of distribution of continuous variables was assessed by visual inspection of the histograms. Discrete variables were analyzed by Fisher's exact test using the Monte Carlo estimation of the exact p-value when appropriate.

Among patients with successful ablation the actuarial probability of freedom from AF after ablation was calculated with the method of Kaplan and Meier. Differences between the curves were tested for significance by the log-rank statistic.

A p value <0.05 was considered statistically significant.

Logistic regression analysis was conducted to study the effects of baseline characteristics, medical history, medication history, left atrial diameter, status of procedure success and study sites on the success of the endpoint. Univariate logistic regression models were conducted for each of the potential predictors. A p-value <0.20 was used for the purpose of screening covariates. Forward, backward and Stepwise selection algorithms were used for selecting the covariates into the multivariate logistic regression model. Only covariates with a p-value <0.05 remained in the final model. Odds ratio and 95% confidence limit were calculated.

Analysis was performed by means of SAS 9.2.

4. Results

Demographic data of the 82 study patients are presented in Table 1. The majority (80.5%) of our patients were male. Most of them suffered from structural heart disease (mainly hypertensive cardiopathy, 57.5%).

4.1. Catheter ablation

PV ablation was electrophysiologically successful in 38/82 (46.3%) patients. There were 77 subjects (77/82, 93.9%) where left atrial linear

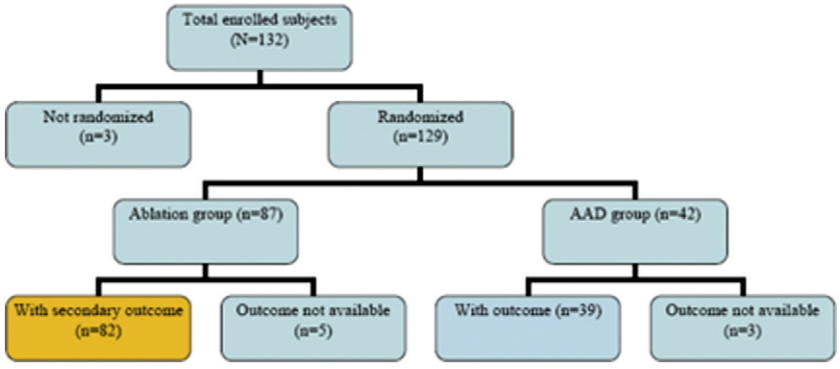

Fig. 1. Diagram of the accountability of subjects.