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Efficacy of cryoballoon ablation in patients with paroxysmal atrial fibrillation without time to pulmonary vein isolation assessment☆

Giuseppe Stabile [a,*], Claudio Tondo [b], Antonio Curnis [c], Maurizio Lunati [d], Massimiliano Manfrin [e], Giulio Molon [f], Luigi Sciarra [g], Massimo Mantica [h], Saverio Iacopino [i], Giuseppe Arena [j], Maurizio Landolina [k], Alberto Arestia [a], Roberto Verlato [l]

[a] Clinica Mediterranea, Napoli, Italy
[b] Cardiac Arrhythmia Research Centre, Centro Cardiologico Monzino IRCCS, University of Milan, Milano, Italy
[c] Azienda Ospedaliera Spedali Civili, Brescia, Italy
[d] Ospedale ASST GOM Niguarda, Milano, Italy
[e] Ospedale Civile di Bolzano, Bolzano, Italy
[f] Ospedale Sacro Cuore Don Calabria, Negrar, Italy
[g] Policlinico Casilino, Roma, Italy
[h] Istituto Clinico Sant'Ambrogio, Milano, Italy
[i] Villa Maria Cecilia, Cotignola, (RA), Italy
[j] Nuovo Ospedale Apuane, Massa, Italy
[k] Ospedale Maggiore, Crema, Italy
[l] ULSS 6 Euganea, Camposampiero, Italy

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ABSTRACT

Background: Real-time visualization of the electrical activity of the pulmonary veins (PV) is not always possible in the setting of atrial fibrillation (AF) cryoballoon ablation. We investigated the relation between the effective documentation of time to PV isolation and the clinical outcome in a cohort of patients with paroxysmal AF who underwent cryoballoon ablation.
Methods: One thousand forty two consecutive patients were enrolled. An inner lumen mapping catheter was typically used to visualize real-time electrical activity inside the PVs.
Results: Time to PV isolation was documented in all targeted PVs in 391 patients (Group 1), in 651 patients it was not possible to record PV potentials and assess time to PV isolation in at least one PV (Group 2). In Group 1 a longer procedure duration and ablation time were observed, while a longer fluoroscopy time was observed in Group 2. After a mean follow-up of 14 ± 11 months, 209/1042 (20%) patients had an atrial arrhythmia recurrence (20.2% in Group 1, 19.9% in Group 2, $p = 0.25$). Complications occurred in 54/1042 (5.2%) patients without any difference among the two study groups.
Conclusion: In our retrospective analysis, in about two thirds of patients undergoing cryoballoon ablation it was not possible to acutely assess time to PV isolation in all PVs. However, one-year freedom from clinically symptomatic atrial tachyarrhythmia was similar to that of patients in which time to PV isolation was documented in all targeted veins.
Clinical Trial Registration: clinicaltrials.gov (NCT01007474).

1. Introduction

Catheter ablation is a well-established therapy for drug refractory atrial fibrillation (AF), and ablation strategies that target pulmonary veins (PVs) are the cornerstone for most AF ablation procedures [1–3]. When targeted, complete electrical PV isolation should be achieved. PV isolation, using an open irrigated catheter, with a point-by-point ablation strategy and a circular mapping catheter to validate it, is the widest used approach for AF catheter ablation [3]. However it can be time-consuming and the clinical results and complications are still depending on center volume and operator experience. To overcome some of these limitations and simplify the catheter procedure different "one-shot" techniques have been developed [4–7]. Among them cryoballoon ablation has emerged as the widest used and its safety

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* Corresponding author at: Laboratorio di Elettrofisiologia, Clinica Mediterranea, Via Orazio 2, 80100 Napoli, Italy.
E-mail address: gmrstabile@tin.it (G. Stabile).

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and efficacy have been demonstrated to be similar to point-by-point ablation radiofrequency [8]. To assess the time to PV isolation and the effective PV isolation, a circular mapping catheter is required. However, real-time visualization of the electrical activity inside the PVs by means of an inner lumen mapping catheter is not always possible in the setting of cryoballoon ablation in patients with AF [9–11].

The aim of our study was to investigate the relation between the effective documentation of time to PV isolation and the clinical outcome in a cohort of patients with paroxysmal AF who underwent cryoballoon ablation.

2. Methods

2.1. Patients selection

The patients included in the present analysis were followed in a network of 30 cardiology centers, which participate in the Italian ClinicalService® framework (Clinical Trial Registration Information: http://clinicaltrials.gov/ct2/show/ NCT01007474), 1STOP project. This is a national medical care project aimed at evaluating and improving the use of medical therapies in the clinical practice. The project consists of a shared environment for the collection, management, analysis, and reporting of data from patients in whom Medtronic therapies have been applied [12]. Patients aged between 18 and 90 years with documented symptomatic paroxysmal AF episodes refractory to antiarrhythmic therapy were eligible for the analysis. Exclusion criteria were: (1) persistent and permanent AF; (2) previous catheter ablation of AF; (3) New York Heart Association functional class IV; (4) unstable angina or acute myocardial infarction within 3 months; (5) need for or prior cardiac surgery within 6 months; (6) contraindication to treatment with oral anticoagulants and (7) severe chronic renal or hepatic impairment.

The project was approved by each site's Medical Ethics Committee or Medical Director and conforms to the principles outlined in the Declaration of Helsinki. Each patient provided informed consent for data collection and analysis.

2.2. Ablation procedure

After transseptal catheterization, the cryoballoon catheter was introduced into the left atrium via a 12F steerable sheath (FlexCath Advance, Medtronic, Inc.). Mapping of the PVs was performed with an inner lumen mapping catheter (Achieve, Medtronic, Inc.). As a default, the 20 mm Achieve catheter was used. The mapping catheter was advanced in each PV ostia, positioned as proximal as possible to provide PV potentials recording. A 28-mm cryoballoon catheter (Arctic Front Advance, Medtronic) was advanced inflated and positioned at each PV antrum. Optimal vessel occlusion was considered to have been achieved when selective contrast injection showed the absence of contrast backflow to the atrium. When complete occlusion could not be achieved, the mapping catheter was replaced by a stiff guide wire (Amplatz Ultra Stiff, Cook Medical, Bloomington, IN, USA).The standard set of lesions includes the left superior pulmonary vein (LSPV) treated as first, followed by the left inferior (LIPV), right superior (RSPV), and right inferior (RIPV). As per nature of this project, we did not implement a standardized protocol on the number and duration of freeze nor the usage of a bonus freeze but a general strategy was shared among the centers. In case of the presence of a common ostium, the veins were treated as separate branches. Target application time was 180–240 s.

Time-to-PV isolation was defined as the time from freeze initiation to the last recorded PV potentials. If the temperature did not attain −40 °C within 60 s or acceptable nadir temperature was not reached, a bonus freeze with a different occlusion was applied. The right phrenic nerve was paced from the superior caval or subclavian vein during freezing at the septal PVs. Phrenic capture was monitored by tactile feedback. In case of cessation or weakening of right hemi-diaphragm contractions, freezing was immediately terminated [9, 13].

2.3. Post-ablation management and follow-up

Oral anticoagulation was left uninterrupted on the day of the procedure for all patients and continued for at least 3 months or long term in patients with a high thromboembolic risk assessed by CHA_2DS_2-VASc score. Antiarrhythmic drugs were usually discontinued ≥5 half-lives prior to ablation, except for amiodarone. Patients were scheduled for follow-up examinations 3, 6, and 12 months after the initial treatment and every 6 months thereafter. Rhythm monitoring during the follow-up visits was performed by the clinical assessment of AF recurrence, ECG and Holter monitoring according to the clinical practice of each center. Patients were asked to provide any other ECG or Holter monitoring performed since the previous visit.

Ablation was deemed successful in the absence of symptomatic or asymptomatic atrial tachyarrhythmias lasting longer than 30 s identified by surface ECG or Holter monitoring. As early relapse of atrial tachyarrhythmias within the first 3 months after catheter ablation may be a transient phenomenon, this transition period was excluded from the final efficacy analysis and denoted as a blanking period [14].

2.4. Aim of the research

The primary endpoint of the analysis was to retrospectively evaluate the clinical outcome of patients in whom time to PV isolation was acutely documented by recording the disappearance of the electrical activity in all targeted PVs (Group 1), compared to that of patients in whom time to PV isolation was not documented in at least one PV (Group 2).

2.5. Statistical analysis

Baseline characteristics and clinical data have been summarized and then compared between the groups using appropriate summary statistics. Variables on a continuous scale have been described as mean, standard deviation, median and interquartile range, minimum and maximum. Variables on a categorical scale were presented as counts and percentages. Summary statistics have been reported with a maximum 2 decimals, as appropriate. Comparisons between groups have been performed using Wilcoxon's Test for continuous variables, while comparisons of categorical variables have been performed by means of the Chi-square test or Fisher exact test for extreme proportions, as appropriate. In case of statistical differences, the two by two comparisons have also been performed and reported. To compare the time-to-first event, survival analysis was carried out by means of the Kaplan-Meier method. The differences between groups were tested by log rank methods and the proportional hazards models were fitted. The annual rates of complications have been reported, together with the 95% Poisson confidence intervals. The Poisson regression model has been used to calculate the incidence rate ratio (IRR), with the d-scale option. To find predictors for AF recurrences, a Cox regression was imputed for both univariate and multivariate analyses. After testing for collinearity, all parameters with a p-value <0.10 in univariate were analyzed then in a multivariate model and a final p-value <0.05 was considered as statistically significant on the outcome. Statistical analysis was performed through SAS 9.4 software (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Study population

One thousand forty two consecutive patients were included in the study. Their baseline clinical characteristics are showed in Table 1.

3.2. Procedural data

Time to PV isolation was documented in all targeted PVs in 391 (37%) patients (Group 1), in 651 (63%) patients time to PV isolation was not documented in at least one PV. In 43 (4%) patients the operator chooses to not use the Achieve catheter or any other mapping catheter to assess the time to PV isolation. The time to PV isolation was not documented, including: (1) in 132/651 (20%) of cases with left superior PV, (2) in 147/651 (22%) of cases with left inferior PV, (3) 148/651 (22%) of cases with right superior PV, and (4) 189/651 (28%) of cases with right inferior PV. The time to PV isolation was not documented in only one PV in 29/651 (5%) patients, in 2 PVs in 397/651 (61%) patients, in 3 PVs in 86/651 (13%) patients, and in all PVs in 139/651 (21%) patients. Table 2 summarizes the main procedural characteristics during the catheter ablation. In Group 1 a longer procedure duration and ablation time were observed, while a longer fluoroscopy time was observed in Group 2. A mean nadir temperature ≤ −40 °C was achieved for all PVs (Table 2).

3.3. Follow-up data

After a mean follow-up of 14 ± 11 months, 209/1042 (20%) patients had an atrial arrhythmia recurrence (79/391 patients, 20.2% in Group 1, 130/651 patients, 19.9% in Group 2, $p = 0.23$). Considering the blanking period, 226/1042 (21.7%) patients had an atrial arrhythmia recurrence (92/391 patients, 23.3% in Group 1, 135/651 patients, 20.7%, in Group 2, $p = 0.33$). The Kaplan–Meier estimation of the time to AF recurrence after the blanking period in the two study groups is shown in Fig. 1. The annual rate of atrial arrhythmia recurrence was 21.49% in Group 1, and 18.9% in Group 2.

A univariate analysis was performed in order to investigate the influence of baseline patient characters on AF recurrence rates. All relevant baseline characteristics were included in the analysis. In the

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