International Journal of Cardiology xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Center experience does not influence long-term outcome and peri-procedural complications after cryoballoon ablation of paroxysmal atrial fibrillation: Data on 860 patients from the real-world multicenter observational project

Maurizio Landolina [a,*], Giuseppe Arena [b], Saverio Iacopino [c], Roberto Verlato [d], Paolo Pieragnoli [e], Antonio Curnis [f], Maurizio Lunati [g], Werner Rauhe [h], Gaetano Senatore [i], Luigi Sciarra [j], Giulio Molon [k], Pietro Maria G. Agricola [a,l], Luigi Padeletti [m,n], Claudio Tondo [o]

[a] ASST Ospedale Maggiore, Crema, Italy
[b] Nuovo Ospedale delle Apuane, Massa, Italy
[c] Maria Cecilia Hospital, GVM Care & Research Group, Cotignola, Italy
[d] ULSS 15 Padovana, in ULSS 6 Euganea, Camposampiero, Italy
[e] Careggi Hospital, Florence, Italy
[f] Azienza Ospedaliera Spedali Civili, Brescia, Italy
[g] ASST GOM Niguarda, Italy
[h] Ospedale Centrale di Bolzano, Divisione di Cardiologia, Bolzano, Italy
[i] General Hospital Ciriè, Torino, Italy
[j] Policlinico Casilino, Rome, Italy
[k] Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy
[l] Casa di Cura Privata Piacenza, Italy
[m] University of Florence, Italy
[n] IRCCS Multimedica, Milano, Italy
[o] Heart Rhythm Center at Monzino Cardiac Center, IRCC Dept. of Clinical Sciences and Community Health, University of Milan, Milan, Italy

ARTICLE INFO

Article history:
Received 17 January 2018
Received in revised form 13 June 2018
Accepted 9 July 2018
Available online xxxx

Keywords:
Atrial fibrillation
Ablation of atrial fibrillation
Cryoablation
Outcomes
AF recurrence

ABSTRACT

Background: The aim of this research was to evaluate whether the procedural data, the incidence of complications, and the long-term freedom from atrial fibrillation (AF) recurrences are influenced by center experience in a paroxysmal AF (PAF) population performing a first-time pulmonary vein isolation (PVI) by cryoballoon ablation (CBA).

Methods: A total of 860 patients underwent PVI by CBA. Center experience groups were predefined according to the quartiles of the distribution regarding the amount of performed procedures: 3.1%, 10.6%, 22.7% and 63.6% of patients were respectively followed in each group from 1st (less experienced) to 4th (more experienced) quartile of experience.

Results: In the entire population, median procedure and fluoroscopy time were 105 and 25 min, respectively. The median procedure time significantly decreased from 130 to 90 min ($P < 0.001$) as the center's experience increased. In 47 (5.5%) patients, a peri-procedural complication occurred. As the experience of centers increased, the acute intraprocedural PVI success rate increased (from 94.3% to 98.9%, $P = 0.007$), whereas there was a tendency towards a decreased incidence of peri-procedure complications (from 7.4% to 4.6%, $P = 0.998$). The mean 1-year freedom from AF recurrence probability was 78.3%, and the 18-month mean was 68.9% with no difference among the groups with different levels of experience.

Conclusion: CBA is a safe and effective treatment for patients with PAF. Peri-procedural complications and procedural times were low in all the analyzed sub-groups, showing a decreasing trend in function of center expertise. The long-term freedom from AF recurrence was not influenced by the level of experience.
(clinicaltrials.gov: NCT01007474)

* Corresponding author at: Department of Cardiology, Ospedale Maggiore di Crema, Largo Ugo Dossena, 2, 26013 Crema, Italy.
E-mail address: maurizio.landolina02@gmail.com (M. Landolina).

https://doi.org/10.1016/j.ijcard.2018.07.051
0167-5273/

1. Introduction

Catheter ablation of atrial fibrillation (AF) has developed from a specialized, experimental procedure into a common treatment to abolish or reduce the recurrence of AF, and pulmonary vein isolation (PVI) has been proven as a cornerstone of catheter ablation [1]. Additionally, the numbers of AF ablations are predicted to rise steeply as a consequence of the increasing number of patients suffering from AF due to an aging population with cardiovascular co-morbidities predisposing to AF (*e.g.*, hypertension, heart failure, coronary artery disease, valvular heart disease, obesity, diabetes mellitus, and/or chronic kidney disease) [1–8].

When performed in experienced centers, AF ablation by PVI has been shown to be more effective than antiarrhythmic drug (AAD) therapy in maintaining sinus rhythm [1,3–5]. More recently, the cryoballoon system has been developed [9] to simplify PVI and facilitate the deployment of these procedures into ablation centers, thus allowing for broader patient access to AF ablation therapy. Consequently, the objective of this research was to evaluate whether the procedural data, incidence of complications, and long-term freedom from AF recurrence could be influenced by a center's experience level when treating patients with paroxysmal AF (PAF) during an index pulmonary vein (PV) cryoballoon ablation (CBA).

2. Methods

2.1. Project organization

Thirty Italian cardiology centers conducted prospective observational research on procedural data, peri-procedural complications, and AF recurrences in patients who underwent an index ablation for symptomatic drug refractory PAF while using CBA. The patient population was divided into four groups according to the experience level of the centers where the CBA procedures were performed. An index score representing the center's level of expertise was denoted as the ratio between the number of performed CBA procedures and the duration of time (in months) when the ablations were performed. This calculation was an estimate of the yearly volume of CBAs conducted at a center. Using predefined quartile settings, the experience level was denoted by four separate categories ranging from the 1st quartile (less experienced) to the 4th quartile (most experienced). After separation into quartiles, there were seven centers in quartile one, seven centers in quartile two, nine centers in quartile three, and seven centers in quartile four.

Data collection was performed in the framework of the ClinicalService "One Shot *TO* Pulmonary vein isolation (1STOP)" project. The 1STOP project is a part of a larger Italian medical care research, The Italian ClinicalService Project (NCT01007474) which is a clinical data repository for an integrated network consortium of Italian cardiac hospitals with the shared goal of evaluating and improving the usage of Medtronic medical therapies in clinical practice through the mutual collection, examination, and analysis of pooled data. In this project, an independent scientific committee of physicians prospectively identifies key clinical questions on a yearly basis for analysis and dissemination. A charter assigns the ownership of data to the centers and governs the conduct and relationship of the scientific committee and Medtronic. Medtronic did not have any role in identifying research objectives, interpreting results, or drafting the manuscript [10]. Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in *a priori* approval by the institution's human research committee.

2.2. Project design and end point

The patients included in this analysis represent a cohort that consecutively underwent PVI by CBA using the second generation cryoballoon (Arctic Front Advance Cardiac CryoAblation Catheter System; Medtronic Inc., Minneapolis, MN, USA) for symptomatic recurrent PAF in 1STOP participating centers from September 2012 to May 2016. Baseline assessments included the collection of demographic information, medical history, data on cardiovascular medication, 12 lead ECG, and AF history. No cryoablation protocol guidelines were provided to the participating centers. Patients were scheduled for follow-up examinations at 3-, 6-, 12- and 18-months after the index ablation. At each follow-up visit, clinical data on AF recurrence were evaluated by 12 lead ECG and 24-hour Holter monitoring. Additionally, the presence of any new adverse event(s) was recorded during each follow-up visit.

Acute procedural success was defined as the ratio between the number of effectively isolated PVs and the number of target PVs. AF recurrence was defined as an electrocardiographically documented episode of AF or atrial tachycardia lasting at least 30 s. Since AAD management following CBA was performed according to each center's practice rather than a standardized protocol, we analyzed long-term AF recurrence, both, in the entire population, regardless of the usage of AAD, as well as, in patients off AAD from the end of the 3-month blanking period. Using a landmark blanking period, recurrences of any atrial arrhythmia within the first 3 months after the procedure were not considered as failure. Complications related to the procedure and/or occurring in the month following the procedure were classified as minor or major according to the criteria used in the worldwide survey on AF ablation [4].

2.3. Statistical analysis

Baseline characteristics and clinical data were examined for normality of distribution and then summarized by statistical methods. Variables on a continuous scale have been described as mean, standard deviation, median/interquartile range, and minimum/maximum values. Variables on a categorical scale were presented as counts and percentages. Summary statistics were reported with a maximum of two decimals, as appropriate. A survival analysis was conducted by means of Kaplan-Meier method. The annual rates of events were reported with the 95% Poisson confidence intervals. In the incidence analysis, the rate of event should be interpreted as the rate of patients with at least one AF recurrence. All tests were 2-sided, and a 2-tailed *P*-value <0.05 was considered statistically significant. To find predictors for AF recurrences, a Cox regression was imputed for both univariate and multivariate analyses. After testing for collinearity, all significant univariate parameters ($P < 0.10$) were analyzed in a multivariate model. A final multivariate *P*-value <0.05 was considered a statistically significant outcome. Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA).

3. Results

Our analysis included 860 patients (265 female; 30.8%) with PAF who underwent CBA after a mean of 54.8 months from the first diagnosis of AF. Baseline clinical characteristics are shown in Table 1. The mean age was 58.1 ± 10.9 years and 319 (37.1%) patients suffered from hypertension. The mean left atrium (LA) diameter was 40.0 ± 5.7 mm, and the mean LA area was 20.9 ± 5.0 cm^2. Out of 860 patients, 3.1%, 10.6%, 22.7% and 63.6% were followed in each group from the first (less expert) to the fourth (more expert) quartile of expertise, respectively. The centers in quartile one performed an average of 45.7 ± 21.6 PVI procedures per year regardless of the energy source, in quartile two the average of PVI procedure increased to 55 ± 38.1, in quartile three to 65 ± 40.2, 3 and in quartile four to 180 ± 119.1. In quartile one, two, and four all centers performed both RF and cryo PVI; whereas, 2% of the centers in quartile three used only cryoenergy for PVI.

Typically, the analysis stratified by center experience showed that more experienced centers treated patients for PVI earlier than less experienced centers as demonstrated by the number of tested AADs and the time from first AF diagnosis (Table 1); however, in general, patients treated in more experienced centers had greater left atrial area compared to those of less experienced centers (Table 1).

3.1. Procedural data

For the whole population, the median procedure duration was 105 min [interquartile range (IQR): 77–135]. The median fluoroscopy time was 25 min (IQR: 18–35), and the median ablation time was 20 min (IQR: 16–32). The distribution of procedural time, fluoroscopic duration, ablation time, and other procedural data as a function of center experience are shown in Table 2. Procedural, fluoroscopic, and ablation time as well as the number of freezes significantly decreased with increasing center experience ($P < 0.001$). The left superior, left inferior, right superior, and right inferior PVs were treated and isolated in 98.6%, 97.8%, 98.9%, and 97.2% of the entire population, respectively. The percentage of effectively treated right PVs significantly increased with the expertise of the centers (Table 2). Specifically, the percentage of effectively treated right inferior PVs ranged from 88.3% to 98.3% ($P < 0.001$) increasing with the center experience. Overall the acute success rate was 98.8%, increasing with the center experience from less experienced to the most experienced (94.3% *vs.* 98.9% respectively, $P = 0.007$).

Out of 860 patients, a complication occurred in 47 (5.5%) patients. No patients experienced an atrioesophageal fistula, stroke, death, or other major peri-interventional complication. In general, there was a tendency towards a decreased incidence of procedure-related complications from quartile 1 and 2 (7.4% and 7.7%, respectively) to quartile

Please cite this article as: M. Landolina, et al., Center experience does not influence long-term outcome and peri-procedural complications after cryoballoon ablation of paroxysmal ..., Int J Cardiol (2018), https://doi.org/10.1016/j.ijcard.2018.07.051