

Preliminary Experience with Cryoballoon Ablation in Paroxysmal Atrial Fibrillation: 100-case series

Experiencia preliminar de crioablación con catéter balón en fibrilación auricular paroxística: serie de 100 casos

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ABSTRACT

Background: The evaluation of novel energy sources for the treatment of paroxysmal atrial fibrillation (PAF) is of great clinical interest. Cryoballoon ablation appears as an attractive alternative for patients with PAF refractory to pharmacological therapy.

Objectives: The purpose of this study was to describe the initial cryoballoon ablation experience performed at our institution from November 2013 to May 2015 in patients with PAF, evaluating the safety, efficacy and characteristics of the procedure.

Methods: This was a retrospective, observational study analyzing the first 100 consecutive cases performed with 28-mm Artic Front™ cryoballoon (Medtronic, Inc.) from November 2013 to May 2015.

Immediate success was defined as isolation of all pulmonary veins.

Atrial fibrillation recurrence was assessed in 72 patients with more than 6 months follow-up.

Results: The procedure lasted 78.03 ± 19.84 min with fluoroscopy duration of 20.79 ± 11.91 min and a total radiation dose of 202.93 ± 81 mGy. The rate of acute success was 100%. The complication rate was 1% due to transient diaphragmatic paralysis. The AF-free rate was 81.95% in patients with over 6-months follow-up.

Conclusions: Our initial experience with cryoballoon ablation was safe and effective with a high rate of acute success and low rate of complications. The procedure was short and the AF-free rate was more than acceptable.

Key words: Atrial Fibrillation - Catheter Ablation - Cryosurgery - Electrophysiology

RESUMEN

Introducción: La evaluación de nuevas fuentes de energía para el tratamiento de la fibrilación auricular paroxística (FAP) es de gran interés clínico. La crioablación con catéter balón se presenta como una alternativa atractiva para los pacientes con FAP refractaria al tratamiento farmacológico.

Objetivos: Describir la experiencia inicial llevada a cabo en nuestra institución desde noviembre de 2013 hasta mayo de 2015 con la utilización de la técnica de crioablación con catéter balón en pacientes con FAP y evaluar la seguridad, la eficacia y las características del procedimiento.

Material y métodos: Estudio retrospectivo observacional de un solo centro en el que se examinaron los 100 primeros casos consecutivos realizados con criobalón Artic Front® de 28 mm (Medtronic, Inc.) desde noviembre de 2013 hasta mayo de 2015.

Se definió éxito inmediato al aislamiento de la totalidad de las venas pulmonares.

La recurrencia de fibrilación auricular se evaluó en el grupo de 72 pacientes que tuvieron un seguimiento de más de 6 meses.

Resultados: La duración del procedimiento fue de $78,03 \pm 19,84$ minutos con un tiempo de fluoroscopia de $20,79 \pm 11,91$ minutos y una dosis de radiación total de $202,93 \pm 81$ mGy. La tasa de éxito inmediato fue del 100%. La tasa de complicaciones fue del 1% a raíz de una parálisis diafragmática transitoria. En el seguimiento de los pacientes con más de 6 meses del procedimiento, la tasa libre de fibrilación auricular fue del 81,95%.

Conclusiones: Nuestra experiencia inicial con crioablación resultó segura y eficaz, con una tasa de éxito inmediato elevada y una tasa de complicación es baja. El procedimiento resultó ser de corta duración y la tasa libre de fibrilación auricular en el seguimiento fue más que aceptable.

Palabras clave: Fibrilación auricular - Ablación con catéter - Criocirugía - Electrofisiología

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Abbreviations

AF	Atrial fibrillation	PAF	Paroxysmal atrial fibrillation
INR	International normalized ratio	RF	Radiofrequency
LMWH	Low molecular weight heparin		

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained arrhythmia in daily practice and its prevalence increases significantly with population age. Clinical studies based on epidemiological data predict two- to three-fold increase of the current disease prevalence by the year 2050. (1)

Catheter ablation for paroxysmal atrial fibrillation (PAF) is the treatment of choice in refractory and symptomatic patients, according to current treatment guidelines. (2) However, the procedure is not without complications, generally described in the literature in the range of 2% to 5%. (3)

Radiofrequency (RF) has become the preferred method for AF ablation, but it has some disadvantages: it disrupts the tissue with risk of thromboembolism; it generates an inhomogeneous lesion with tissue fibrosis, which could lead to pulmonary vein stenosis, and increases perforation and atrio-esophageal fistula risk. (4) Regarding success rate, a recurrence of about 30% has been reported, which is an issue that worries the groups devoted to treat these arrhythmias. (5-6)

Therefore, the assessment of new sources of energy that may overcome these limitations and potentially improve outcomes in terms of efficacy is of great clinical interest. An alternative source of energy is cryothermic energy. (7) Clinical studies have revealed that cryoenergy determines a transmural, homogeneous lesion, with no endothelial damage preserving the histoarchitecture of the underlying tissue. (8) Therefore, lesions are minimally thrombogenic, with low risk of pulmonary vein stenosis (9, 10) and lower risk of perforation. However, phrenic nerve paralysis appears as the most frequent complication, with higher incidence with second generation cryoballoons, though reversible in most cases. (11) The aim of this study was to evaluate the safety, efficacy, and success rate of cryoballoon ablation procedures, which began to be used in our center in 2013.

METHODS

Design, population and management prior to ablation

This is an observational retrospective, single-center (Instituto Cardiovascular de Buenos Aires) study including the first 100 consecutive cases of symptomatic PAF refractory to treatment with at least one anti-arrhythmic drug, who underwent PAF ablation with 28 mm Arctic Front® cryoballoon (Medtronic, Inc) from November 2013 to May 2015.

Exclusion criteria were: persistent AF, secondary AF, congestive heart failure, severe valve failure or stenosis, congenital heart diseases, anticoagulation contraindication, presence of thrombus in the left atrium, pregnancy or serious comorbidities.

Patients received oral anticoagulation therapy with the new oral anticoagulants, warfarin or acenocoumarol, and were controlled with the international normalized ratio (INR) in a range between 2.0 and 3.0 in the last two cases. Warfarin or acenocoumarol were discontinued 3 half-lives prior to the procedure and replacement with low molecular weight heparin (LMWH) was prescribed. In the case of new anticoagulants they were suspended three half-lives prior to the procedure without performing bridge with LMWH.

Prior to ablation, all patients underwent high-resolution cardiac 64-slice computed tomography to determine left atrial anatomy as well as pulmonary vein conduit and diameter. It is important to emphasize that the presence of a common pulmonary trunk was not an absolute contraindication for the procedure in our series; only patients with ostium diameter >28 mm were excluded.

Procedure

All procedures were performed under general anesthesia.

Two femoral vein punctures were performed to introduce a DAIG deflectable decapolar catheter (St. Jude Medical, Inc.), which was positioned in the coronary sinus, and an Across transeptal puncture sheath (St. Jude Medical, Inc.).

Prior to transeptal puncture, intravenous heparin was administered and during the whole procedure anticoagulation was maintained with activated clotting time ≥ 300 ms, monitored at 20-minute intervals.

Once the transeptal puncture was performed a guide-wire was positioned in the left superior pulmonary vein removing the puncture sheath. Then, a flexible 15 Fr Flex-Cath sheath with its dilator (Cryo-Cath Technologies) was introduced, and its distal portion was positioned in the left atrial cavity in a 40° left anterior oblique projection. A balloon catheter over an Achieve octapolar circular mapping catheter (Medtronic, Inc.) was advanced through this sheath and electrograms were recorded within each vein, confirming the presence of pulmonary vein potentials and their isolation during the procedure.

Catheter employed

A first generation Arctic Front cryoballoon catheter was employed in the first 36 cases and the remaining 64 cases were performed with a second generation Arctic Front Advance cryoballoon catheter. Both were 10.5 Fr double-lumen balloon catheters (CryoCath Technologies, Montreal, Quebec, Canada) (Figure 1) allowing the circulation of nitrous oxide at temperatures of -30°C to -75°C , a cooling gas that absorbs the heat of the surrounding tissue, resulting in its freezing. After each application, the gas is evacuated to the exterior of the system.

The cold source is released through a console with adjusted monitor providing temperature attained and application time.

Each of the veins was catheterized with the 28-mm diameter balloon catheter, adjusted to the PV antrum to achieve good targeted occlusion, with contrast retention of 50% within the vein and no leak to the atrial cavity (Figure 2).

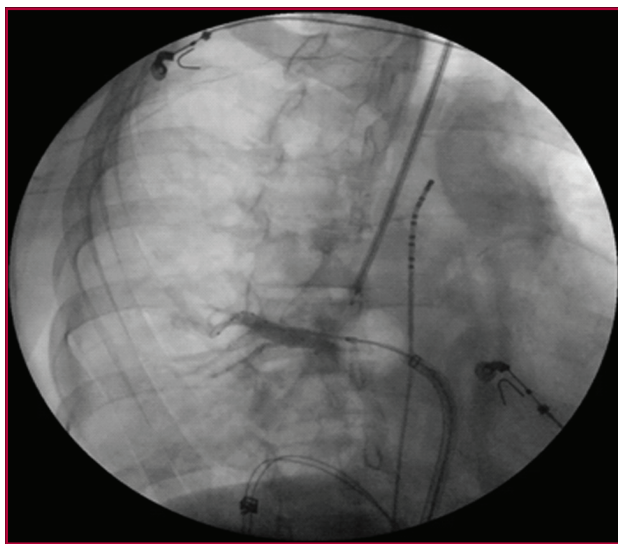


Fig. 1. Radioscopy showing pulmonary vein occlusion with cryoballoon.

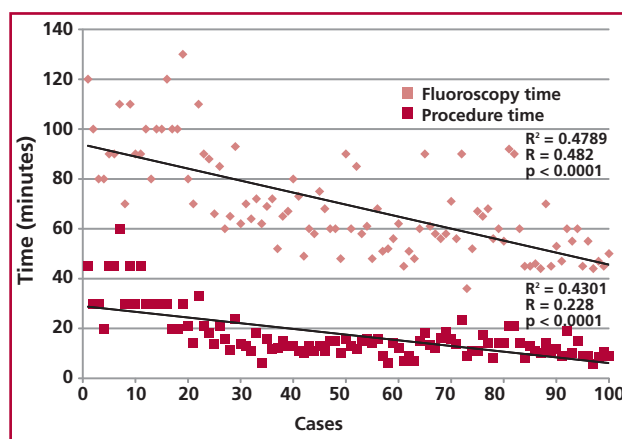


Fig. 2. Relationship between the number of procedures performed and fluoroscopy time.

Once verified, the freezing process was initiated, keeping balloon pressure against the vein for 90 seconds; after this time, the balloon was completely adhered to the PV antrum, and the freezing process was continued for a total of 240 seconds. Cold was applied between 2 and 3 times to each vein.

In all cases, intracardiac echocardiography to monitor complications and Doppler to assess pulmonary vein occlusion were performed.

After both superior and inferior left vein ablation, the decapolar catheter was positioned in the superior vena cava for continuous phrenic nerve stimulation at a frequency of 60 beats/min (1000 ms cycle.), in order to monitor phrenic nerve integrity during cryoablation of the right pulmonary veins, especially the superior veins.

In all cases esophageal temperature was monitored, avoiding temperatures below 20 °C. Additionally, in all cases phrenic nerve stimulation was performed in order to decrease nerve injury.

Acute procedural success was defined as pulmonary vein isolation with bidirectional block.

After the procedure, and once the entire system was removed from the intravascular space, anticoagulation was reversed with protamine.

Post ablation management and follow-up

Patients remained hospitalized in the intensive care unit for 24 hours after the procedure, and were discharged the following day.

Anticoagulation was resumed six hours post procedure with intravenous heparin in continuous infusion and then continued with oral anticoagulation for 3 months. All antiarrhythmic drugs were resumed after the procedure and suspended 3 months post ablation.

Patient follow-up consisted of visits to the Atrial Fibrillation Clinic at months 1, 2, 3, 6, 9, and 12 after the procedure, including a medical interview, physical examination, chest x-ray, 12-lead ECG and 24-hour Holter monitoring.

Statistical analysis

Discrete variables are expressed as percentages and continuous variables as mean or median with their corresponding standard deviation or interquartile range, according to their distribution. The chi square test was used to compare discrete variables and Student's t test or the Mann-Whitney test for continuous variables, matching sample distribution. A p value <0.05 was defined as statistically significant. The Kaplan-Meier method was used to assess AF-free rate.

All data were analyzed using SPSS 21.0 software package.

Ethical considerations

The protocol was reviewed and approved by the institutional Ethics Committee. Since this is a retrospective study, no informed consent was required (CABA Law N° 3101). According to Argentine Law No.25326 on protection of personal data, all information will remain confidential.

RESULTS

The study included 100 patients (76 men and 24 women) with mean age of 53.83±13.54 years, and documented history of recurrent, symptomatic PAF, refractory to antiarrhythmic therapy, of 2-6 year evolution. The CHA₂DS₂-VASC score was 1 (1-3).

Ninety one per cent of patients had no structural heart disease and left ventricular ejection fraction was 55±5.39%. The average left atrial area was 20.68±4.19 cm² and its diameter 41±3 mm (Table 1).

Procedure time was 78.03±19.84 min and cryoablation time 36±4 min (Table 2).

Table 1. Population characteristics

Male gender, %	76
Age, years	53.83±13.54
PAF, %	100
EF, %	55±5.39
Left atrial area, cm ²	20.68±4.19
Structural cardiomyopathy, %	9
CHA ₂ DS ₂ -VASC score	1 (1-3)

PAF: Paroxysmal atrial fibrillation. EF: Ejection fraction

Immediate success rate was 100%, with a first attempt occlusion rate of 73%, an interval between onset of cryoenergy application to vein isolation of 60 ± 29 seconds, trough temperature achieved at 30 seconds of -31 ± 3 ° C and mean temperature attained in every vein of -40.04 ± 6 ° C.

Complication rate was 1% and only due to phrenic paralysis, reversing after one month post ablation.

Regarding the learning curve, there was an acceptable and significant correlation between the number of procedures performed and fluoroscopy and total procedure times (see Figure 2).

To analyze AF recurrence only patients with at least 6-month follow-up were included. These included 72 patients with median follow-up of 10.50 (7.5-12) months and AF-free rate of 81.95% without antiarrhythmic drugs (Figure 3). Sixty-one patients were followed-up for more than 1 year.

DISCUSSION

Our initial experience in PAF cryoballoon ablation was safe with a low rate of complications and accept-

able success, both in immediate vein isolation as in AF mid-term recurrence.

Cryoballoon ablation is considered an attractive alternative to RF. Numerous studies have shown that this technique may achieve complete circular lesions around the pulmonary veins without damaging the endothelium, reducing complication risks such as pulmonary vein perforation or stenosis. In our work, no esophageal perforations or pulmonary stenosis occurred during follow-up. We presented one diaphragmatic paralysis due to right phrenic nerve lesion which reversed before one month. This complication has a reported incidence of up to 24%, mostly temporary, reversing within 24 h after the procedure. (11) It is possible that by using phrenic nerve stimulation and the diaphragmatic palpation technique for early diagnosis of phrenic nerve injury, this type of lesions can be prevented. In 8 patients in whom this phenomenon was observed, the application was suspended and the cryoballoon repositioned, thus avoiding phrenic nerve paralysis.

The reduced endothelial damage caused by cryoablation does not imply less effectiveness, since it has been demonstrated that 98% acute isolation of the pulmonary veins is immediately achieved. In our experience isolation was completed in 100% of cases and, as reported, the right inferior pulmonary vein was the most difficult to isolate, although special techniques (“hockey stick”, “pull-down” or “big loop”) helped to achieve isolation in all cases, without using a focal catheter.

Cryoablation is associated with significantly short-

Table 2. Technical characteristics of the procedure

Mean procedure time, min	78.03 ± 19.84
Mean fluoroscopy time, min	20.79 ± 11.91
Mean fluoroscopy dosage, mGy	202.93 ± 81
Mean temperature attained in each vein, C°	-40.04 ± 6
Mean temperature at 30 seconds, C°	-31 ± 3

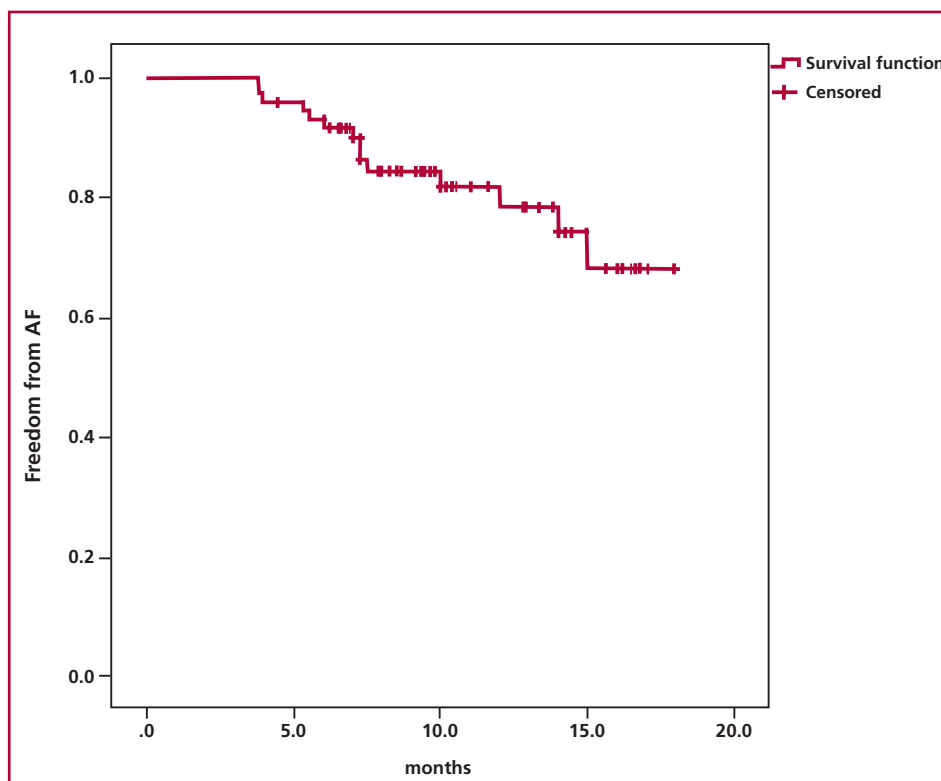


Fig. 3. Patients free of atrial fibrillation (AF) at follow up

er procedure times than those performed with RF. In our initial experience mean procedure time were 78.03 ± 19.84 min, which is similar to that reported by other authors. (4, 7, 8) This leads to lower anesthesia time and better procedure tolerance. This time decreased as our operators gained experience with the technique.

Regarding the arrhythmia-free rate achieved during follow-up, our figures are similar to the experiences of international centers, but we must be cautious considering that it is a mid-term follow up. (4, 9, 11, 15)

In conclusion, our initial experience with PAF cryoablation has been more than satisfactory and represents the most important one published in Latin America hitherto. Probably the analysis of more cases and longer follow-up will allow us to detect long-term success and complication predictors, as well as decrease the total procedure time.

Limitations:

This is a retrospective, single-center study where the procedures were performed by two different operators.

The results obtained with first and the second generation balloons are not discriminated in this study.

This work presents the mid-term follow-up of patients after the procedure and this might explain the high maintenance rate of sinus rhythm.

CONCLUSIONS

Our initial experience with cryoablation proved to be safe and effective in treating symptomatic PAF refractory to medical therapy, with a high rate of immediate success and low complication rate. The procedure was short and the AF-free rate during follow-up is more than acceptable.

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Conflicts of interest

None declared

(See author's conflicts of interest forms in the web / Supplementary Material)

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