Cryoballoon atrial fibrillation ablation: Single-center safety and efficacy data using a novel cryoballoon technology compared to a historical balloon platform.

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Abstract

Introduction: Catheter ablation is superior to drugs regarding atrial fibrillation (AF) recurrence, symptoms improvement, and mortality reduction in heart failure. POLARx is a novel cryoballoon, with technical improvements seeking to improve outcomes. So far, its clinical evidence is restricted to a case report. Methods: To compare the POLARx cryoballoon procedural safety and efficacy to the already established Arctic Front Advance PRO (AFAP) in a single-center cohort study, consecutive patients undergoing AF cryoablation with the POLARx were enrolled. Data were prospectively gathered. POLARx patients were compared to a historical cohort of patients submitted to AF cryoablation with the AFAP. Results: Seventy patients were analyzed, 20 in POLARx, and 50 in the AFAP group. They all underwent first-time pulmonary vein isolation, 77% were male, 94% had paroxysmal AF, median age was 62.5 years, median CHA2DS2-VASc 1, left-atrium size 34ml/m^2, and 65% were receiving anticoagulation. The primary end-point, all pulmonary veins isolation, was 100% in both groups. The complication rate was similar (0% POLARx vs. 5.7% AFAP, p=0.39). The median total procedural time was longer in the POLARx group (90min vs. 60min, p<0.001), but the overall time-to-isolation (TTI) (44.8sec vs. 39sec, p=0.253) and ablation time (15min vs. 13.7min, p=0.122) was similar between POLARx and AFAP groups, respectively. Despite equal TTI, the POLARx had a lower minimal temperature reached (-57oC vs -47oC, p<0.001). Conclusion: The novel POLARx cryoballoon had similar efficacy and safety compared to the AFAP. It was also associated with longer procedural times, similar TTI, and lower minimum temperature reached.

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia worldwide. According to the Global Burden of Disease study, it affects 33.5 million individuals and its incidence is increasing every decade[1]. Consequences are cerebrovascular events, heart failure, impaired quality of life, and increased mortality[2,3]. Multiple trials have shown that catheter ablation is superior to antiarrhythmic drugs in reducing AF recurrence, alleviating symptoms, and mortality, in heart failure context[4–6].

Cryoablation is a valid option for the classical point-by-point radiofrequency (RF) pulmonary vein isolation (PVI), with well-designed, randomized studies showing its non-inferiority when compared to RF catheter ablation[7,8]. The Medtronic's cryoballoon (CB) overtime passed through many modifications seeking to improve quality. Compared to the first-generation CB Arctic Front (CB-1) (Medtronic, Minneapolis, USA), Arctic Front Advance (CB-2) (Medtronic, Minneapolis, USA) presented enhanced distal hemisphere free-

zing, leading to a higher rate of acute PVI, shorter procedural times, and comparable safety[9]. The Arctic Front Advance ST (CB-3) (Medtronic, Minneapolis, USA) had a shorter distal nose-tip on the balloon, what facilitated the real-timed assessment of pulmonary vein potentials[10]. Currently, most AF cryoablations are performed using the Arctic Front Advance PRO system (Medtronic, Minneapolis, USA), the 4th generation device, characterized by better catheter maneuverability and ergonomics, achieving shorter procedural times[11].

Recently, the POLARx (Boston Scientific, Marlborough, MA, USA) cryoballoon received CE-Mark and started to be used in Europe. The system has the same cryoablation workflow of the state-of-the-art cryoablation technology, with some improvements to, theoretically, improve outcomes. So far, its clinical evidence is restricted to a case report[12]. Thus, we decided to perform this study comparing the POLARx CB to the already established Arctic Front Advance PRO.

Methods

Study Population

The cohort study consisted in prospectively collecting data of the first 20 patients undergoing PVI for AF with the novel POLARx CB. They were compared to a historical cohort took from a study that evaluated the Arctic Front Advance PRO balloon (CB-4) against its previous version[13]. The option for choosing this particular group of controls was due to convenience and completeness of the clinical and procedural data available. In this case, the whole CB-4 group had data gathered for comparison. The project and data collection activities conform to the principles outlined in the Declaration of Helsinki, and each patient included provided informed written consent. The study was approved by the local Institutional Committee on Human Research.

Aims of the study

This study aims to evaluate the efficacy and safety of the POLARx CB, comparing it to the established Arctic Front Advance PRO. The chosen primary endpoint was acute success, defined as success in electrically isolating all the four veins in the procedure. Secondary outcomes were: complications rate, procedural duration, fluoroscopy time, ablation time, time-to-isolation (TTI), lowest temperature reached, number of veins isolated with a single cryo cycle, and high-sensitive troponin I (hs-TnI) level 24 hours after the procedure.

Procedural workflow

All the procedures were performed under deep sedation. A decapolar was positioned in the coronary sinus and a quadripolar in superior vena cava (SVC). Intravenous unfractionated heparin was administered (100 UI/kg), aiming for an activated clotting time (ACT) between 350-450 seconds. Standard fluoroscopy-guided transseptal puncture was performed, and the standard SL0 sheath was changed over-the-wire for a Flexcath 15Fr or a POLARSHEATH 16Fr. The veins were ablated following the sequence: left superior pulmonary vein (LSPV), left inferior pulmonary vein (LIPV), right inferior pulmonary vein (RIPV), and right superior pulmonary vein (RSPV). The vein occlusion was checked with contrast dye injection. The freezing time duration and the number of attempts for each vein, as well as additional lesions or procedures, were left to the operator's discretion. Usually, applications would vary from 180 to 300 sec, without bonus freeze. During ablation, vein potentials were monitored in real-time whenever possible by a circular wire-catheter (Achieve or POLARMAP). When right pulmonary veins were ablated, the right phrenic nerve was paced through the SVC catheter, and diaphragmatic movements were closely monitored by upper-abdomen palpation or movement sensor in case of POLARx, triggering immediate freezing stop in case of ceasing or weakening of diaphragmatic movements. Esophageal temperature was monitored throughout the procedure. An esophageal temperature of less than 18^{o}C would trigger immediate freeze cessation. After ablation, entrance block was confirmed by the absence of vein potentials, and exit block by failure in capturing the left atrium by stimulating inside the vein with maximum output. The POLARx console screen and gears are displayed in **figure 1** . To see in detail the freezing-thawing process using the POLARx system, together with the built-in diaphragm movement sensor, watch the **video 1** in supplementary material. Twenty four hours

after ablation all patients had hs-TnI levels measured.

Statistical analysis

Continuous variables were evaluated for normality using the Shapiro-Wilk test. Due to their non-normal distribution, they were described as median (Q1-Q3). Mann-Whitney U test was used for comparisons between them. Categorical variables were expressed as number (%) and were analyzed using the Chi2-test or Fisher's exact test. Since this is an exploratory study, with no equal previous study, no sample size calculation was performed. Statistical tests were based on a two-sided significance level of 0.05. SPSS statistical software v.23.0 (IBM, Armonk, NY, USA) was used for all statistical analyzes.

Results

A total of 70 patients were analyzed in this study, 20 from the POLARx group, enrolled from 12th August 2020 to 30th October 2020; and 50 from the Arctic Front Advance PRO, sampled from a cohort of a previously published study (from October 2018 to February 2019). Their median age was 62.5 years, the majority were male (77.1%), had paroxysmal AF (94.3%), a median LA size of 32 ml/m2, and CHA_2DS_2-VASc 1. Except for hypertension, the baseline clinical characteristics were similar between groups. All patients were undergoing their first PVI procedure. Details about baseline clinical characteristics can be seen in **table 1** . The primary efficacy endpoint, acute success, was obtained in 100% of patients in both groups. No patients had necessity to undergo touch-up ablation with RF to complete vein isolation. Complications occurred exclusively in the Arctic Front Advance PRO group, but in a small number [0 vs. 4 (8%), p =0.39], among them, 3 self-limited phrenic palsies and a post-procedural pericardial effusion without necessity for intervention. Compared to Medtronic's CB, POLARx, in this cohort, was associated with a longer procedure (90 min vs. 60 min, p <0.001), lower minimum temperature (-57oC vs. -47.5oC, p <0.001), lower TTI temperature (-44oC vs. -32oC, p <0.001), but similar TTI (44.8 sec vs. 39 sec,p <0.001). The median number of veins isolated in the first attempt, per patient, was also lower in POLARx CB (3 vs. 4,p <0.001). Overall 27.1% of patients underwent a combined procedure, mostly cavotricuspid ablation line for typical atrial flutter (84.2% of the combined procedures). No difference in the hs-TnI level collected 24 hours after the procedure was observed between groups. The full procedural details are displayed in **table 2** . They are also displayed as plot in **figure 2** .

Discussion

To the best of your knowledge, this is the first clinical study comparing the novel POLARx CB to the already established Arctic Front Advance PRO.

Briefly, we found that the POLARx CB had a similar profile in terms of efficacy and safety when compared to the Medtronic's CB. Despite achieving all veins isolation by the end of the procedure in 100% of the patients, the POLARx CB demanded a higher procedural time and had a lower number of veins isolated in the first attempt. Interestingly, the cryoenergy application time was the same. A possible explanation for that could be the lack of experience with some of the new features and workflow of the POLARx, an issue intrinsic to the first procedures with new devices. Notwithstanding the similarities between tools and procedural workflow, some differences in the practical handling were consensus between our operators. The POLARSHEATH introducer, although 1Fr larger, tended to cross the septum more easily and smoothly due to its more gradual taper from the dilator to the sheath. We also had the feeling that the set sheath plus balloon was softer and more flexible when compared to the Flexcath plus CB. This can be seen as an advantage since it allows easier vein cannulation, or disadvantage once it can make more difficult to reach vein occlusion. Another point against the novel CB is the impossibility to perform the pull-down maneuver. This is due to a build-in sensor of balloon dislodgement aiming to enhance procedural safety. When the CB is pulled to seal the inferior vein segment, the system often detects it as an involuntary CB displacement and it stops the cryoenergy delivery immediately, hindering a maneuver commonly used to seal the vein.

An interesting finding is the difference found in the minimum temperature reached. The median lowest temperature and temperature reached when the vein turned isolated was approximately 10oC lower in the

POLARx group. Despite that, the TTI was similar between groups, and so does the troponin level. These findings point to a non-different tissue damage, making us theorize that the temperature inside the atrial tissue does not differ between groups, and that this temperature difference may be due to a different way or location where it is measured. Since we did not perform routinely pre or post voltage map, we were not able to evaluate acute and/or chronic scar extension. In one of the POLARx patients, we performed successfully, besides PVI, posterior wall isolation exclusively using the CB; the result can be seen in a previous publication[12].

No complication was observed in the 20 POLARx cases, and 4 minor complications were observed in the Arctic Advance PRO group: 3 temporary phrenic nerve palsies and a pericardial effusion without hemodynamic compromise. Since, fortunately, as in other AF cryoablation cohorts, our complication incidence was low, we could not draw significant conclusions about group differences. Another interesting feature of POLARx is the possibility to monitor diaphragm contraction with the diaphragmatic movement sensor (DMS), a sensor that shows it in real-time as a quantified number in percentage. If even a reduction in diaphragm contraction is detected it triggers a red warning sign, allowing earlier cryoenergy delivery stop. Unfortunately, it is not always possible to use the DMS together with hand palpation, since the pressure applied by the hand cause error in the DMS reading, as can be seen in **video 1** (supplementary material). The summary of pros and cons of both technologies is available in **figure 3** .

Owing to the fact that POLARx has just entered the market in Europe, no data from previous studies is available to be compared with ours. But, taking into account previous studies comparing different CB generations, we observe that evolution is possible and desired. Since the release of the first generation (CB-1), Medtronic improved the design 3 times, being born: Arctic Front Advance (CB-2), Arctic Front Advance ST (CB-3), and lastly, the Arctic Front Advance PRO (CB-4). A real-world study evaluating 480 patients, 120 in each generation group, found a progressive reduction in procedural duration (150 min, 95 min, 90 min, 75 min, from CB-1 to CB-4, as well as a reduction in fluoroscopy time and ablation duration, with the same success rate. This denotes that even if reaching a higher success was not possible, the evolution in balloon architecture improved the handling, making the procedure easier[11].

Summarizing, our study found that the novel POLARx CB had similar efficacy and safety compared to the Arctic Front Advance PRO CB. It also achieved lower temperatures, but with similar TTIs. However, it was associated with a longer procedure and a lower number of pulmonary veins isolated in the first attempt. The DMS for phrenic monitoring is useful and has the potential to make the procedure safer.

Limitations

Among the limitation are its non-randomized study design, the small sample size since the new balloon has just entered the market, and the impossibility to blind the operator once each catheter has marked physical differences. In this study, a follow-up study was not possible because we performed the last cases a few weeks before writing the manuscript.

Conclusion

The novel POLARx cryoballoon had similar efficacy and safety when compared to the Arctic Front Advance Balloon. Since this is the first study to evaluate it, future studies with larger sample sizes are necessary to confirm our findings, especially about a possible reduction in complications.

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FIGURES LEGENDS

Figure 1. POLARx system

In the left upper panel: the POLARx cryoballoon and POLARMAP circular diagnostic catheter. In the center upper panel: the POLARSHEATH steerable sheath. In the lower panel: The SMARTFREEZE console screen. In the right side: the console and the pedal used to inflate/deflate the balloon and to initiate/stop cryoenergy delivery.

Figure 2. Boxplots showing procedural data

Figure 3. Pros and cons of both technologies

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