Safety and efficacy of a second-generation cryoballoon in the ablation of paroxysmal atrial fibrillation

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BACKGROUND Compared with the first-generation Arctic Front cryoballoon (ARC-CB), the new Arctic Front Advance cryoballoon (ARC-Adv-CB) increases the efficient CB-tissue contact surface during freezing, which may increase the incidence of phrenic nerve (PN) palsy (PNP).

OBJECTIVE To evaluate the safety and efficacy of paroxysmal atrial fibrillation (AF) ablation with the ARC-Adv-CB as well as the merits of a predictor of PNP.

METHODS AF ablation was performed by using a "single 28-mm big CB" approach. The rate of pulmonary vein (PV) isolation with a first cryoapplication was measured. The distance between the CB and a PN pacing catheter in the superior vena cava was measured to predict PNP during freezing.

RESULTS In 147 patients, PV were isolated with a single cryoapplication in 205 (81.3%) of 252 PV treated with the ARC-CB and in 280 (90.3%) of 310 PV treated with the ARC-Adv-CB ($P = .003$). The mean time to PV isolation was 52 ± 34 seconds and 40 ± 25 seconds ($P < .001$) and the temperature at the time of isolation was −36.1 ± 10.3°C and −32.3 ± 10.2°C ($P = .001$) in the ARC-CB and ARC-Adv-CB groups, respectively. Mean procedure and fluoroscopy durations were significantly shorter in the ARC-Adv-CB group. Transient PNP was observed in 7(10.6%) and 20(24.4%) of the patients treated with the ARC-CB and ARC-Adv-CB, respectively ($P = .048$). The distance between the lateral edge of the CB and a vertical line through the tip of the pacing catheter accurately predicted PNP ($P < .001$).

CONCLUSIONS The 28-mm ARC-Adv-CB enabled more efficient ablation of paroxysmal AF and shorter procedures than did the ARC-CB. This higher performance was associated with a higher incidence of PNP, which was predicted by the distance between the CB and the PN.

KEYWORDS Cryoablation; Paroxysmal atrial fibrillation; Cryoballoon ablation; Pulmonary vein; Pulmonary vein isolation; Phrenic nerve palsy

ABBREVIATIONS **AF** = atrial fibrillation; **AP** = anterior-posterior; **ARC-Adv-CB** = Arctic Front Advance cryoballoon; **ARC-CB** = Arctic Front cryoballoon; **CB** = cryoballoon; **CI** = confidence interval; **LA** = left atrial; **LIPV** = left inferior pulmonary vein; **PN** = phrenic nerve; **PNP** = phrenic nerve palsy; **PV** = pulmonary vein; **PVI** = pulmonary vein isolation; **RIPV** = right inferior pulmonary vein; **RSPV** = right superior pulmonary vein; **Se** = sensitivity; **Spe** = specificity; **SVC** = superior vena cava

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Introduction

After the discovery of ectopic activity in the pulmonary veins (PVs) as a major trigger, complete PV isolation (PVI) became first-line therapy for paroxysmal atrial fibrillation (AF).[1,2] Although, because of its high success rate, radiofrequency energy remains the most frequently used technique for the ablation of paroxysmal AF, it is generally agreed that point-by-point ablation around the PV ostia is highly complex, time-consuming, and sometimes the source of major complications.[3,4] Cryothermal ablation with cryoballoons (CBs) enables the PVI sometimes with a single application and is safe, straightforward, and associated with a steep learning curve.[5,6] Its immediate and 1-year rates of successful PVI are similar to those of radiofrequency ablation.[7–9] Phrenic nerve (PN) palsy (PNP), the main complication of CB ablation, usually occurs with the use of 23-mm CBs that can be advanced farther inside the right-sided PVs.[10,11]

The performance of safer, more antral ablation procedures using a "single big CB" approach was described by Chun et al.[5] The first-generation Arctic Front CB (ARC-CB; Medtronic, Inc, Minneapolis, MN) was coolest at the balloon's equator. Consequently, even with a tight occlusion, the CB had to be perfectly centered inside the PV antra to

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create complete lesions. Liu et al[12] underscored this limitation and hastened the development of the second-generation Arctic Front Advance CB (ARC-Adv-CB; Medtronic, Inc) equipped with a homogeneous refrigerant system on the distal pole of the CB. Since this new design is likely to be more adaptable to atypical anatomies or imperfect CB applications, improving its overall efficacy,[13,14] one may expect an increase in the incidence of PNP because of deeper freezing and the ice cap that persists after deflation of the CB.[15]

This nonrandomized study was performed to compare the procedural safety and efficacy of the ARC-CB with that of the ARC-Adv-CB in the treatment of highly symptomatic paroxysmal AF. We also examined the merits of a potential predictor of PNP.

Methods

This study was performed according to local institutional regulations, and all patients granted their written informed consent to participate.

Between August 2011 and July 2013, consecutive patients presenting with highly symptomatic, paroxysmal AF resistant to ≥ 1 antiarrhythmic drug(s) were included in this study. They were excluded if they presented with a history of persistent AF, left atrial (LA) ablation, or surgery or with a prosthetic heart valve, an LA thrombus, or a $\geq$28-mm-wide or $\geq$10-mm-long, right or left common PV trunk. Patients enrolled between August 2011 and September 2012 were treated with the ARC-CB, while patients enrolled between August 2012 and June 2013 were treated with the ARC-Adv-CB, when it became available.

Ablation procedure

Before the ablation procedure, a transesophageal echocardiogram was performed to exclude the presence of an LA thrombus and measure the LA dimensions and left ventricular ejection fraction. The computed tomography of LA was performed to examine the PV anatomy. Vitamin K antagonists or other oral anticoagulants were discontinued. All procedures were performed under conscious sedation using midazolam and fentanyl as necessary. A 6F Xtrem quadripolar catheter (Sorin SPA, Milan, Italy) was placed in the coronary sinus via the right femoral vein. A single transseptal puncture was performed under fluoroscopic and pressure guidance. Thereafter, heparin was administered intravenously to maintain an activated clotting time between 250 and 350 seconds. A single big CB approach using a 28-mm CB was performed as described previously.[5] The CB catheter was introduced into the left atrium through a 12F FlexCath steerable sheath (Medtronic, Minneapolis, MN) constantly flushed with heparinized saline. Finally, an Achieve mapping catheter (Medtronic) was advanced over the CB to the PV orifice and positioned as proximally as possible inside the vessel to record the PV potentials at baseline and monitor the isolation procedure in real time. Then, the CB was inflated and advanced to the ostium of each PV. The quality of vascular occlusion was ascertained by the injection of diluted contrast material into the PV and graded from 1 to 4 as mild, medium, subtotal, or total. Once the best occlusion was obtained, cryothermal energy was applied for 300 seconds with the ARC-CB and for 240 seconds with the new ARC-Adv-CB, as recommended by the manufacturer. An additional application of energy was systematically delivered after PVI, unless PNP was observed.

Before ablation of the right-sided PVs, the quadripolar catheter was relocated to the superior vena cava (SVC) to constantly pace the right PN at a 2000-ms cycle length and 20-mA output during freezing. In the case of cessation or weakening of the right hemidiaphragmatic contraction, freezing was immediately discontinued and the CB was deflated.

In a subset of 40 patients, we measured before the isolation of right-sided PVs with the ARC-Adv-CB, the distance between (1) a vertical line crossing the distal SVC PN pacing catheter and (2) the lateral edge of the CB in an anterior-posterior (AP) view, using the 28-mm equatorial diameter of the CB before the initiation of freezing as a reference measurement. We also divided the CB and its surrounding space into 4 zones to facilitate and hasten the assessment of its relationship with the PN (Figure 1; from the right to the left of the patient, respectively: zone A: right side out of CB toward right PVs; zone B1: distal pole of CB from the lateral edge to its center; zone B2: proximal pole of CB from the center to its left extremity; zone C: left side, out of CB). The CB was separated in 2 zones (B1 and B2) for

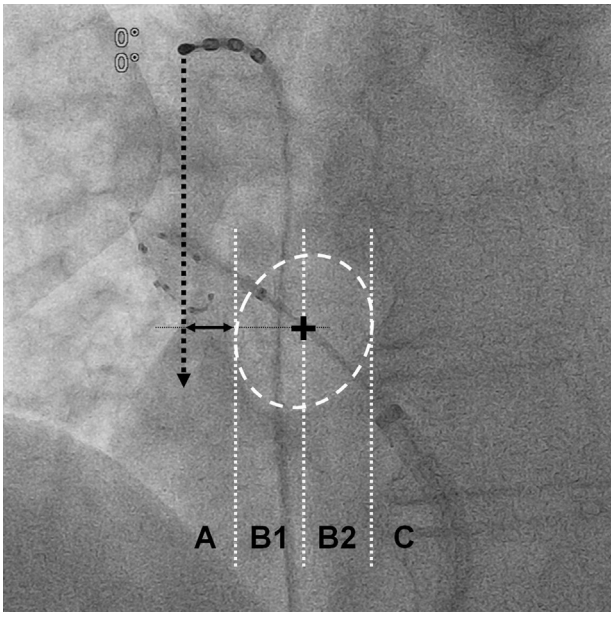

Figure 1 Phrenic nerve-CB relationship in the anterior-posterior view. The distance between the black dotted line and the lateral edge of the CB was measured (bidirectional arrow). Four zones were defined from the right to the left of the patients: zone A: right side outside the CB toward the right pulmonary veins; zone B1: distal pole of the CB from the lateral edge to its center; zone B2: proximal pole of the CB from the center to its left border; zone C: left side outside the CB. CB = cryoballoon.