Cryoballoon Ablation for Pulmonary Vein Isolation in Patients With Persistent Atrial Fibrillation
One-Year Outcome Using Second Generation Cryoballoon

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**Background**—Data regarding the freedom from atrial fibrillation (AF) in the follow-up of persistent AF patients is limited. The second-generation cryoballoon has better cooling properties compared with first-generation cryoballoon. In this study, we aimed to assess the medium-term efficacy of second-generation cryoballoon in patients with persistent AF.

**Methods and Results**—A total of 100 patients (63±10 years, 80% male) with symptomatic persistent AF, despite ≥1 antiarrhythmic drug(s), who were scheduled for pulmonary vein isolation using second-generation cryoballoon were enrolled in this study. Follow-up was based on outpatient clinic visits, including Holter ECGs. Recurrence was defined as a symptomatic or documented arrhythmia episode of >30 seconds excluding a 3-month blanking period. As a result, 393 pulmonary veins (7 patients with common ostium) were successfully isolated. Mean procedural and fluoroscopy times were 96.2±21.3 and 19.7±6.7 minutes, respectively. Phrenic nerve palsy occurred in 3% (3/100) of the patients. At a mean follow-up duration of 10.6±6.3 months, 67% of the patients were in sinus rhythm. Stepwise multivariable Cox proportional hazard regression analysis showed that early AF recurrence (hazard ratio 3.83, 95% confidence interval 1.91–7.68, *P*<0.001) was the only independent predictor for late AF recurrence apart from other clinical and echocardiographic variables.

**Conclusions**—Our findings indicated that second-generation cryoballoon use is associated with favorable outcomes in patients with persistent AF. Recurrence at blanking period was the only predictor of long-term AF recurrence. (Circ Arrhythm Electrophysiol. 2015;8:1073-1079. DOI: 10.1161/CIRCEP.115.002776.)

**Key Words:** cryoballoon ablation ■ persistent atrial fibrillation ■ pulmonary vein isolation

Atrial fibrillation (AF) is the most common sustained tachyarrhythmia seen in 1% to 2% of the general population. Catheter ablation of AF via pulmonary vein (PV) isolation (PVI) is a widely used therapeutic option in selected patient groups. Recent years witnessed an increasing trend for catheter ablation of AF using cryoballoon technique, and successful results are reported regarding the patients with paroxysmal AF. Moreover, the success rate of PVI is reported as high as 80% with second-generation cryoballoon. Cryoballoon ablation is also being increasingly performed in patients with persistent AF; however, long-term success rate is not well known.

Second-generation cryoballoon (Arctic Front Advance, Medtronic Inc, Minneapolis, MN) is a safe and effective method for PVI in AF patients. The novel cryoballoon has several advantages over the first generation in terms of better design, including more optimal cooling and larger lesion formation via forming a hemispheric zone rather than equatorial, and increased injection ports providing more homogeneous freezing capability. Despite these developments, second-generation cryoballoon is not without limitations, such as increased ratio of phrenic nerve palsy (PNP), which is attributed to the better cooling properties of novel cryoballoon.

Although an increasing interest has already developed regarding the efficacy of AF ablation in persistent patients, follow-up data in those patients using novel cryoballoon is limited. In a recent study, Ciccone et al reported the freedom from atrial tachyarrhythmia as 60% after persistent AF ablation with the novel cryoballoon. In this study, we aimed to assess the efficacy of second-generation cryoballoon in a larger group persistent AF patient as an index procedure. We also aimed to report the predictors of recurrence and the change in symptomatic severity during the follow up in this group of patients.
WHAT IS KNOWN

- Cryoballoon ablation is a safe and effective therapy for pulmonary vein isolation in patients with AF.
- Despite the preliminary results of recent studies, the role of cryoballoon ablation in the management of persistent atrial fibrillation is not extensively evaluated.

WHAT THE STUDY ADDS

- One-year results of second-generation cryoballoon indicated favorable outcomes in patients with persistent AF in a large group of patients.
- The pulmonary vein isolation using second-generation cryoballoon without additional linear lesions in left atrium is a possible therapy option in patients with persistent AF.

Methods

Study Population

Between August 2012 and July 2014, patients with symptomatic persistent AF, despite ≥1 antiarrhythmic drug(s) (AAD), who were scheduled for PVI using second-generation cryoballoon were enrolled in this observational study. AF episodes that are sustained beyond 7 days or requiring pharmacological or electric cardioversion or patients with <1 year AF and a rhythm control strategy was beyond 7 days or requiring pharmacological or electric cardioversion were excluded in this observational study. AF episodes that are sustained in the past were the exclusion criteria for the study. Baseline characteristics were recorded for all patients. Symptomatic severity of the patients was recorded according to the European Heart Rhythm Association (EHRA) score. Informed consent was taken from each patient before enrollment. The study was in compliance with the principles outlined in the Declaration of Helsinki and approved by the Institutional Ethics Committee.

Preprocedural Management

All patients underwent transthoracic echocardiography within 1 week before ablation to assess structural abnormality, left ventricular ejection fraction, LA diameter, and valvular disease. Transesophageal echocardiography was performed to rule out presence of thrombus in the LA appendage at the same day of the procedure. In patients under anticoagulation treatment with vitamin K antagonists, the International Normalized Ratio was evaluated. In International Normalized Ratio levels of 2 to 3, the treatment was not ceased. If the patient is using novel oral anticoagulants, then novel oral anticoagulants are discontinued 24 hours before the procedure. Antiarrhythmic drugs were discontinued 5 half-lives before the procedure.

Ablation Procedure With Cryoballoon

Ablation was performed under deep sedation using boluses of midazolam and fentanyl and continuous infusion of propofol. Oxygen saturation and ECG were monitored throughout the procedure. All patients underwent the procedure in sinus rhythm, and if the patient had AF before the procedure, electric cardioversion was performed. Right femoral vein punctures were performed with Seldinger technique. First of all, rotational angiography was performed with an Artis C-arm system (Siemens, Erlangen, Germany) to delineate the left atrial anatomy with PVs. Afterward, a 6 Fr steerable decapolar catheter and nonsteerable catheter were placed in the coronary sinus and His region, respectively. Single transeptal puncture by modified Brockenbrough technique (BRK-1, St.Jude Medical) was performed under fluoroscopy, and 8.5 Fr transseptal sheath (Biosense Webster) was placed into the LA. Once LA access was obtained, left atrial and PV angiography was performed at left anterior oblique 45° and right anterior oblique 30° in patients with a poor image quality in rotational angiography. The sheath was then exchanged with a 12 Fr steerable transeptal sheath (FlexCath, Medtronic CryoCath) over a 0.032 inch guidewire. Afterward, heparin boluses were repeatedly administered to maintain the activated clotting time between 300 and 350 seconds. A 28-mm second-generation cryoballoon catheter (Arctic Front Advance, Medtronic Inc, Minneapolis, MN) was used in the study population. During the procedure, the Achieve mapping catheter (Medtronic, Minneapolis, MN) was positioned in the PV where baseline PV potentials were recorded. The cryoballoon was placed to all PVs by Achieve mapping catheter. Assessment of balloon occlusion was performed by injecting contrast agent through the catheter’s central lumen. Optimal vessel occlusion was considered in case of contrast retention with flow back into the LA, and afterward ablation procedure was started. The duration of each freezing cycle was 240 seconds. In cases of incomplete isolation of PV, additional freezing cycles were applied until complete isolation was achieved. A safety freeze of 240 seconds was applied as a bonus freeze after successful isolation of PVs. The procedure systematically began with the left superior PV, followed by the left inferior PV, right superior PV, and right inferior PV, respectively. To avoid PNP, the decapolar catheter was inserted into the superior vena cava, and diaphragmatic stimulation was achieved by pacing the ipsilateral phrenic nerve with a 1000 ms cycle and a 12 mA output. Phrenic nerve capture was monitored by intermittent fluoroscopy, tactile feedback was obtained after placement of the operator’s hand on the patient’s abdomen, and compound motor action potential was obtained by placing right arm electrode 5 cm above the tip of xiphoid process and left arm electrode along the right costal margin with a 16 cm distance from the right arm electrode. A decrease in compound motor action potential amplitude of 35% was accepted as a significant value to interrupt the procedure in concordance with other methods.

Postprocedural Management

A transthoracic echocardiography was performed immediately after the procedure to exclude the presence of pericardial effusion. All patients were followed up for at least 24 hours in the telemetry unit. Patients were then discharged if their clinical statuses were stable. Oral anticoagulation was initiated in the evening of ablation unless pericardial effusion was detected and continued for at least 3 months after the procedure. Antiarrhythmic drug treatment was also continued for at least 3 months, and the decision to retreatment with AADs after 3 months was given according to the recurrence of atrial tachyarhythmia because of physician’s decision.

Follow-Up

After discharge from the hospital, enrolled patients were scheduled for visits in the outpatient clinics at 1, 3, 6, and 12 months after ablation and every 6 months thereafter, or earlier, if symptoms consistent with recurrent AF developed after the ablation. At each visit, patients were evaluated for the recurrence of arrhythmias with physical examination, questioning for arrhythmia-related symptoms (palpitations, chest discomfort, fatigue, and dizziness), and a 12-lead ECG. A 7-day Holter recording was conducted at third and sixth months, and all of the patients were scheduled for a 24-hour Holter recording at the 1st year. If the patient had complaints compatible with recurrence at clinical visits, additional Holter recordings were also performed. Additionally, telephone calls were made at the end of the follow-up period before analysis. The need for further oral anticoagulation was evaluated in the third month based on the CHA2DS2-VASc score. Any episode of AF, atrial flutter, or atrial tachycardia lasting at least 30 seconds was defined as recurrence. A blanking period of 3 months was considered for the study. Any recurrence occurring in the blanking period was classified as an early recurrence, whereas recurrence after the blanking period was considered as late recurrence.
Statistical Analysis

Normally distributed continuous parameters were presented as mean±standard deviation, and skewed continuous parameters were expressed as median (interquartile range defined as Q1–Q3). Categorical data were presented as frequencies and percentages and were compared using χ² test. Comparisons between baseline characteristics were performed by independent Student’s t test, Mann–Whitney rank-sum, Fisher exact, or χ² tests where appropriate. To analyze the association of baseline and procedural factors on AF recurrence, univariate Cox regression analysis was used. Parameters that are found to be univariately associated with the outcome and those that show a slight association with the outcome with P<0.25 are included in the multivariable Cox regression analysis. Kaplan–Meier analysis was performed to describe AF-free survival. Statistical analyses were performed using SPSS statistical software (version 21.0; SPSS Inc., Chicago, IL). A 2-tailed P<0.05 was considered statistically significant.

Results

Baseline Characteristics

In this study, 100 patients (63±10 years, 80% male) with the diagnosis of persistent AF (94% persistent, 6% long-standing persistent) were enrolled. In the whole study group, 61% of the patients had hypertension, 8% had diabetes mellitus, 27% had dyslipidemia, and 15% had coronary artery disease. Age (62±12 versus 63±9 years, P=0.607), sex (male, 76% versus 82%, P=0.596), history of hypertension (59.4% versus 62.7%, P=0.826), diabetes mellitus (9.1% versus 7.5%, P=0.778), coronary artery disease (18.2% versus 13.4%, P=0.560), and dyslipidemia (30.3% versus 25.4%, P=0.637) did not significantly differ between patients with and without recurrence. Additionally, left atrial diameter (31.7±6.0 cm² versus 33.1±6.1 cm², P=0.262) and left ventricular ejection fraction (58.1%±6.7% versus 57.4%±6.3%, P=0.640) were similar between the 2 groups with (33/100 patients) and without (67/100 patients) AF recurrence. The mean duration of persistent AF was 5.5±3.7 months. Baseline clinical and demographic characteristics of the study population are shown in Table 1.

Procedural Characteristic

In all patients, PVI was performed using a 28 mm cryoballoon. Total procedural time was 96.2±21.3 minutes, and total fluoroscopy time was 19.7±6.7 minutes. Mean number of cryoballoon applications per each PV, except bonus freeze, was as follows: left superior PV, 1.9±0.7; left inferior PV, 1.9±0.7; right superior PV, 1.6±0.6; and right inferior PV, 1.6±0.6, respectively. Mean temperature reached during the procedure per each PV was as follows: −49.7°C±7.3°C for left superior PV, −44.3°C±7.1°C for left inferior PV, −51.5°C±7.2°C for right superior PV, and −46.9°C±7.5°C for right inferior PV, respectively. Acute procedural success rates were 100% for the entire study population. There was no significant difference between patients with and without recurrence relevant to procedural characteristics. Detailed procedural characteristics are shown in Table 2.

Complications

The most frequent complication was vascular access problems. Six patients (6%) had only hematoma in the right groin, which resolved spontaneously, and 4 (4%) patients had pseudoaneurysm, one of which required surgical treatment. PNP occurred during right superior PV ablations. PNP developed in 3 (3%) of our patients, and in 2 of those patients, PNP was transient and completely resolved during the intervention. In cases with transient PNP, we proceeded to right inferior PV ablation. In the patient with persistent PNP, right PVs had common ostium; therefore, we stopped the procedure after PNP. However, the PV signals were already isolated before PNP development. None of the patients died or had a cerebrovascular event in the periprocedural period. Three (3%) patients had postprocedural mild pericardial effusion, which resolved spontaneously, and no pericardial tamponade was observed.

Procedural Outcomes

Compared with baseline values, the symptomatic status of the patients evaluated by EHRA score improved both in patients with and without AF recurrence after cryoballoon ablation (2.9±0.6 versus 2.1±0.6, P=0.001 in patients with recurrence; 2.9±0.5 versus 1.3±0.4, P<0.001 in patients without recurrence). Despite this improvement in EHRA score in patients with AF recurrence, the improvement in EHRA score is better in patients without recurrence compared with that in recurrent AF patients (P<0.001) as illustrated in Figure 1.

The mean follow up duration was 10.6±6.3 months. Among them, 24 (24%) patients had early AF recurrence within the first 3 months of follow-up after the index
cryoballoon ablation procedure. Patients with early AF recurrence had a higher incidence of late AF recurrence in the follow-up compared with those who had no early AF recurrence (45.5% versus 13.4%, respectively, \( P = 0.001 \)). Freedom from AF during a mean follow-up period of 10.6±6.3 months was 67% after cryoballoon ablation when a 3 month blanking period was considered (Figure 2). We observed recurrence in 33 patients in our study population. Among patients with recurrence, 12 (36%) of them had paroxysmal AF, 15 (45%) of them had persistent AF, and 6 (19%) of them had atrial tachycardia. Among those 67 patients without recurrence, only 4 of them were under antiarrhythmic therapy at the last

### Table 2. Procedural Characteristics of the Study Group

<table>
<thead>
<tr>
<th>Variables</th>
<th>All Population (n=100)</th>
<th>No (n=67)</th>
<th>Yes (n=33)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSPV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum temperature, °C</td>
<td>−49.7±7.3</td>
<td>−49.4±7.4</td>
<td>−50.6±7.3</td>
<td>0.446</td>
</tr>
<tr>
<td>Mean number of applications</td>
<td>1.9±0.7</td>
<td>2.0±0.6</td>
<td>1.7±0.7</td>
<td>0.065</td>
</tr>
<tr>
<td>LIPV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum temperature, °C</td>
<td>−44.3±7.1</td>
<td>−44.0±7.1</td>
<td>−45.0±7.4</td>
<td>0.499</td>
</tr>
<tr>
<td>Mean number of applications</td>
<td>1.9±0.7</td>
<td>2.0±0.8</td>
<td>1.7±0.6</td>
<td>0.059</td>
</tr>
<tr>
<td>RSPV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum temperature, °C</td>
<td>−51.5±7.2</td>
<td>−51.7±7.4</td>
<td>−51.2±7.0</td>
<td>0.744</td>
</tr>
<tr>
<td>Mean number of applications</td>
<td>1.6±0.6</td>
<td>1.7±0.7</td>
<td>1.6±0.6</td>
<td>0.365</td>
</tr>
<tr>
<td>RIPV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum temperature, °C</td>
<td>−46.9±7.5</td>
<td>−47.9±8.1</td>
<td>−45.0±5.7</td>
<td>0.064</td>
</tr>
<tr>
<td>Mean number of applications</td>
<td>1.6±0.6</td>
<td>1.6±0.6</td>
<td>1.5±0.6</td>
<td>0.148</td>
</tr>
<tr>
<td>Common ostium</td>
<td>7 (7)</td>
<td>5 (7.4)</td>
<td>2 (6.1)</td>
<td>0.859</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phrenic nerve palsy</td>
<td>3 (3)</td>
<td>1 (1.4)</td>
<td>2 (6.1)</td>
<td>0.498</td>
</tr>
<tr>
<td>Femoral pseudo aneurysm</td>
<td>4 (4)</td>
<td>2 (2.9)</td>
<td>2 (6.1)</td>
<td>0.821</td>
</tr>
<tr>
<td>Total procedural time (minutes)</td>
<td>96.2±21.3</td>
<td>96.2±21.1</td>
<td>96.3±22.3</td>
<td>0.979</td>
</tr>
<tr>
<td>Total fluoroscopy time (minutes)</td>
<td>19.7±6.7</td>
<td>18.9±6.5</td>
<td>21.4±7.1</td>
<td>0.158</td>
</tr>
<tr>
<td>Total fluoroscopy dosage (( \mu )Gym2)</td>
<td>8746.4 (923.5–12739.6)</td>
<td>8256.2(923.5–9739.6)</td>
<td>9598.5(3096.2–12739.6)</td>
<td>0.446</td>
</tr>
</tbody>
</table>

Numeric parameters were expressed as mean±standard deviation or median (min–max). Categorical data were presented as %. LIPV indicates left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; and RSPV, right superior pulmonary vein.

**Figure 1.** Change in European Heart Rhythm Association (EHRA) score in the study group before and after the cryoballoon ablation.

**Figure 2.** Freedom from atrial fibrillation during a mean follow-up period of 10.6±6.3 months after second-generation cryoballoon ablation when a 3 month blanking period considered.
control visit. Baseline demographic, clinical, procedural, and follow-up characteristics regarding the outcome after cryoablation are shown in Table 3.

The univariate Cox proportional hazard modeling of the late AF recurrence after the index cryoablation is showed in Table 3. Among the several clinical and procedural characteristics, only early recurrence at third month predicted late AF recurrence (hazard ratio 3.83; 95% confidence interval 1.91–7.68, \( P < 0.001 \)). Stepwise multivariable Cox proportional hazard regression analysis showed that early AF recurrence was the only independent predictor for late AF recurrence.

**Discussion**

Our 1-year findings indicated that 67% of the persistent AF patients were free from symptomatic AF recurrence after PVI using second-generation cryoballoon. Recurrence of AF at blanking period was the single predictor of recurrence after the index PVI. These findings in such a large patient group are compatible with the data regarding the better efficacy with this novel cryoballoon.

PVI is the cornerstone of catheter ablation of AF, especially in paroxysmal and persistent AF patients.\(^9\)–\(^11\) Although previous studies documented a higher success rate with second-generation cryoballoons in patients with paroxysmal AF, there is little data in persistent AF evaluating the recurrence rates using new generation cryoballoon. Studies evaluating the follow-up after PVI using first-generation cryoballoon revealed lower success rates in persistent AF. In a previous study, the reported success rate of cryoballoon ablation with first-generation cryoballoon was 50% in patients with persistent AF at a median of 18 (6–27) months follow-up.\(^12\) However, second-generation cryoballoon was found to have better outcomes compared with first-generation device among patients with both paroxysmal and persistent patients.\(^3\)\(^,\)\(^4\)

Recently, Metzner et al\(^7\) evaluated 1-year outcomes both in paroxysmal and persistent patients with second-generation cryoballoon, which revealed an improved success rate of 77% in a limited number of short-term persistent AF patients. However, different from other studies, Ciccone et al\(^8\) evaluated 1-year clinical outcomes in a larger patient population, including only persistent AF patients using second-generation cryoballoon as an index procedure, and they reported a success rate of 60%. Those findings indicated better clinical outcomes with second-generation cryoballoon in persistent AF, despite a lower success rate compared with paroxysmal AF.

Similar to recent published data, in our study, the freedom from recurrence at a mean follow-up period of 10.6±6.3 months was better in persistent AF patients. According to our findings, recurrence in the blanking period is the single predictor of long-term freedom from AF. Different from previous studies, LA size was not found to be a significant predictor of outcome in our study population. This might be because of the characteristics of the study population enrolled in our analysis. In addition, minimal temperature at the targeted PV or number of applications was not found as a significant predictor of recurrence.

Several significant improvements became evident in clinical practice with the use of second-generation cryoballoons, including better acute and chronic success rate and decreased fluoroscopy time.\(^4\) It is well known that, besides isolation of PV ostium, 28 mm-balloons are associated with larger lesion formation causing substrate modification, including rotors as well, which has a role in the persistency of AF.\(^13\) In addition, larger lesions might also cause ganglionated plexi.

### Table 3. Univariate and Multivariable Cox Proportional Hazard Analysis of Recurrence After Cryoballoon Ablation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariate analysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.99</td>
<td>0.95–1.02</td>
<td>0.648</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>0.80</td>
<td>0.36–1.78</td>
<td>0.592</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.83</td>
<td>0.41–1.68</td>
<td>0.608</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.24</td>
<td>0.37–4.06</td>
<td>0.722</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1.36</td>
<td>0.64–2.87</td>
<td>0.412</td>
</tr>
<tr>
<td>History of CAD</td>
<td>1.37</td>
<td>0.56–3.34</td>
<td>0.477</td>
</tr>
<tr>
<td>Size of LA</td>
<td>0.96</td>
<td>0.90–1.02</td>
<td>0.185</td>
</tr>
<tr>
<td>LVEF</td>
<td>1.03</td>
<td>0.97–1.09</td>
<td>0.332</td>
</tr>
<tr>
<td>Early recurrence</td>
<td>3.83</td>
<td>1.91–7.68</td>
<td>( \textbf{0.001} )</td>
</tr>
<tr>
<td>LSPV minimum temperature</td>
<td>0.98</td>
<td>0.94–1.03</td>
<td>0.576</td>
</tr>
<tr>
<td>LIPV minimum temperature</td>
<td>0.99</td>
<td>0.94–1.03</td>
<td>0.657</td>
</tr>
<tr>
<td>RSPV minimum temperature</td>
<td>1.01</td>
<td>0.96–1.06</td>
<td>0.608</td>
</tr>
<tr>
<td>RIPV minimum temperature</td>
<td>1.04</td>
<td>0.99–1.09</td>
<td>0.078</td>
</tr>
<tr>
<td><strong>Multivariable analysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early recurrence</td>
<td>3.83</td>
<td>1.91–7.68</td>
<td>( \textbf{0.001} )</td>
</tr>
</tbody>
</table>

CAD indicates coronary artery disease; EHRA, European Heart Rhythm Association; LA, left atrium; LIPV, left inferior pulmonary artery; LVEF, left ventricular ejection fraction; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary artery; and RSPV, right superior pulmonary vein.
modification, which was found to be associated with lesser recurrence rates. Moreover, better cooling properties relevant to the design of the new generation cryoballoon, including formation of an hemispheric cooling zone rather than equatorial and increased injection ports, is thought to provide more antral lesion formation in addition to improved ostial isolation, which is translated into better clinical success and decreased recurrence rates.

Although cryoballoon characteristics are improved, the recurrence rates are not negligible in the studies, including persistent AF patients. Despite improved lesion formation compared with first-generation balloons, a relatively higher rate of recurrence might raise questions regarding the efficacy of one index procedure for long-term clinical success in persistent AF patients. An important concern while evaluating the freedom from arrhythmias in patients with persistent AF is the mode of recurrence. Although acute clinical success is comparable in paroxysmal and persistent AF, higher rate of recurrence in persistent AF might not be solely attributed to conduction recovery at PV ostium. This was also shown in the recent studies, raising concerns about the role of non-PVI sources providing the mechanism for recurrence. In addition, the pattern of conduction recovery in our patient population who underwent a redo procedure using either cryoballoon or 3-dimensional mapping systems is aimed to be evaluated in another study.

Our study findings have some important clinical implications. First, our results are in line with recently published studies with a higher rate of freedom from atrial arrhythmia. Moreover, our findings expand the literature in terms of a larger patient population included. In addition to the recurrence rates, symptomatic status of the patients was also evaluated, which revealed significant improvements in patients free from AF. Moreover, improvement in EHRA score was also observed among the patients with recurrence. However, whether this improvement was as a result of decreased AF frequency or a placebo effect because of an index intervention was not known. The complication rate was also low without any pericardial tamponade or cerebrovascular events and with only one femoral pseudoaneurysm necessitating surgery. During the procedure, in addition to intermittent fluoroscopic control and tactile feedbacks taken from the patients’ abdomen, we also used phrenic nerve monitoring with diaphragmatic compound motor action potential to predict PNP as soon as possible. PNP was observed in only 3% of the patients, which was also comparable with other studies using cryoballoon.

Our study has some limitations. First, this is a single-center, nonrandomized study evaluating the efficacy and safety of primarily second-generation cryoballoon without comparison to other methods. Although our study has the highest patient group reported, large-scale randomized studies are needed both to confirm and expand these data. Second, recurrence was evaluated with 7-day Holter at the third month and sixth month control and 24-hour recordings thereafter. Long-term monitoring with loop recorders might give more accurate data regarding recurrence rates in this patient population.

In conclusion, using second-generation cryoballoon in patients with persistent AF ablation as an index procedure is associated with improved outcomes. Recurrence at blanking period was an important predictor of recurrence in our patient group, similar to previous studies. Further studies are needed to evaluate both safety and efficacy of the novel cryoballoon in persistent AF as an index procedure.

Disclosures
Dr Buelent Koektuerk is the consultant of Medtronic Company. The other authors report no conflicts.

References


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