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Posterior box isolation as an adjunctive ablation strategy during repeat ablation with the second-generation cryoballoon for recurrence of persistent atrial fibrillation: 1-year follow-up

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Abstract

Background The creation of a posterior box isolation of the left atrium (LAPWI) in addition to pulmonary vein isolation (PVI) with the second-generation cryoballoon (CB-A) seems to offer promising clinical outcome in patients affected by persistent atrial fibrillation (PersAF).

Aim This work aims to study the clinical outcome of an ablation strategy based on the creation of a LAPWI during repeat procedures for recurrent AF after an index CB-A procedure for PersAF.

Methods and results A total of 33 patients having undergone a repeat procedure consisting in redo PVI plus LAPWI for recurrent PersAF with the CB-A after an index PVI ablation were retrospective included in our study. Electrical reconnection could be documented in 18 veins (13%). The LAPW was successfully isolated solely by CB-A ablation in 30 out of 33 (91%) patients; in the remaining 3 patients, isolation of the LAPW was completed by focal tip-irrigated RF ablation. The mean number of CB-A applications required for the superior portion of the LAPW and the inferior portion of the LAPW creation were 5.4 ± 0.9 and 4 ± 0.6, respectively. After a mean follow-up of 11.8 ± 3 months, 28 patients (85%) did not experience recurrence of any atrial arrhythmias during follow-up, without the need of further ablation or class I or III AADs.

Conclusion Left posterior wall isolation with the CB-A is feasible and safe during repeat ablation procedures for recurrent PersAF. In our study, the 12-month freedom from any arrhythmia was 85% following this ablation strategy.

Keywords Cryoballoon · Persistent atrial fibrillation · Ablation · Pulmonary vein isolation · Repeat procedures

1 Introduction

The second-generation cryoballoon (CB-Adv) (Arctic Front Advance, Medtronic, Minnesota, USA) has proven to be highly effective in achieving freedom from atrial fibrillation (AF) [1–7]. Recently published data seems to indicate that this procedure might also be effective in the treatment of persistent AF (PersAF) [8, 9]. In addition, substrate modification of the LA using the cryoballoon in adjunction to pulmonary vein isolation (PVI) seems to be feasible and affords promising clinical outcome [10, 11]. In the current manuscript, we studied the clinical outcome of an ablation strategy based on re-isolation of the PVs, if electrically reconnected, and the creation of a posterior box during repeat procedures for recurrent AF after an index CB-A procedure for PersAF (Fig. 1).

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2 Methods

2.1 Aim of the study

The main aim of the study was to describe the clinical outcome in patients who underwent a second ablation procedure with a novel strategy based on the creation of a posterior box

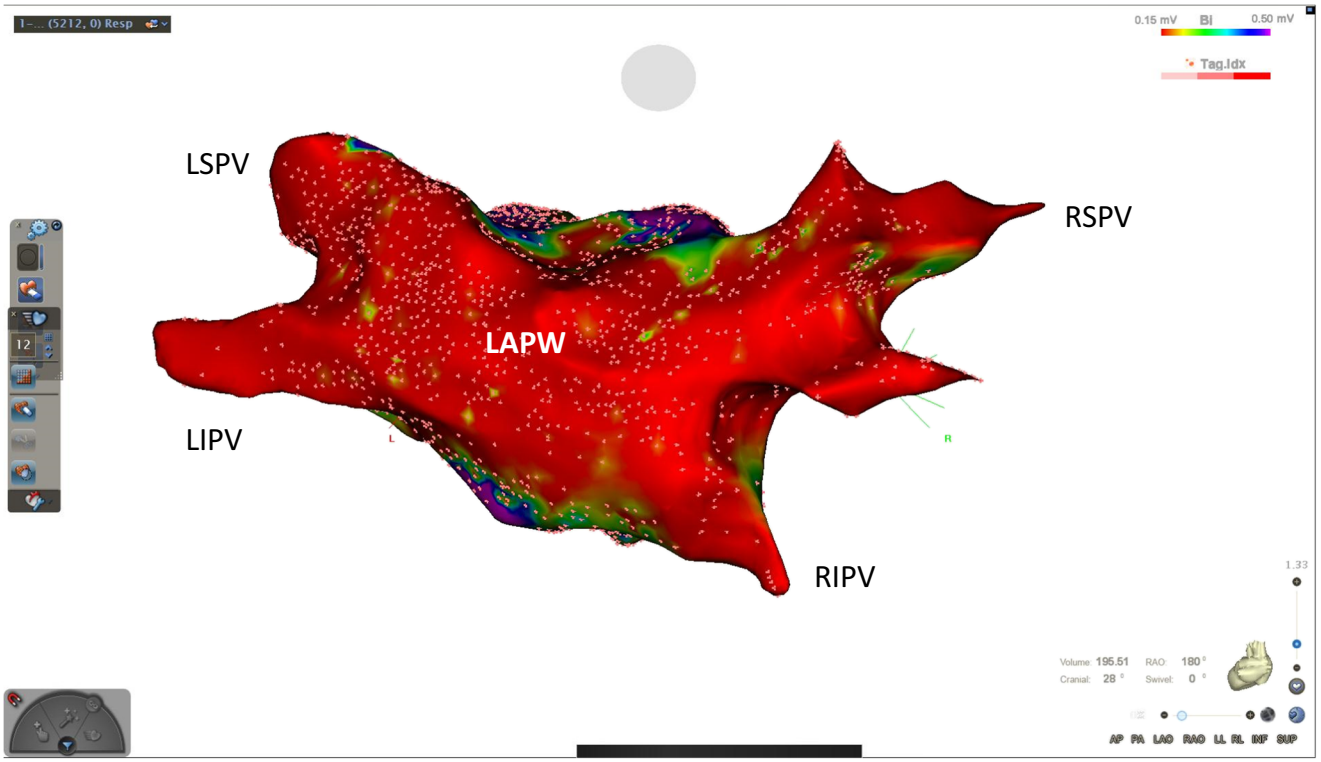

Fig. 1 Postablation images in sinus rhythm recorded with the 3D mapping system. The red region represents voltage < 0.15 mV. LAPW, left atrium posterior wall; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein

with the CB-A for recurrent AF following an index ablation for PersAF with the same technology.

2.2 Study population

The study cohort consisted of consecutive patients who underwent a repeat procedure for recurrent AF after an index procedure with the CB-Adv for the treatment of PersAF at the Heart Rhythm Management Center, UZ Brussels, Belgium, as of 2017. The exclusion criteria were the following: recurrence of paroxysmal atrial fibrillation, non-treated coronary artery disease, intracavitary thrombus, significant valvular disease, contraindications to general anesthesia, and repeat ablation with RF energy. The study was approved by the local ethics committee of our Institution.

2.3 Preprocedural management

All patients provided written informed consent to the ablation procedure. A transthoracic echocardiogram (TTE) was performed within 1 week prior to ablation enabling assessment of structural heart disease. To exclude the presence of thrombi, trans-esophageal echocardiography (TEE) was performed the day before the procedure. All patients underwent a preprocedural CT scan to assess detailed LA and PV anatomy. All anti-arrhythmic drugs (AAD) were discontinued at least 3 days before ablation, apart from amiodarone that was stopped 1 month before. For patients who were receiving treatment with one of the NOAC agents, our practice was to stop anti-coagulation the day prior to ablation. For warfarin, uninterrupted administration was preferable. All patients gave informed consent to the procedure.

2.4 Index procedure

After having obtained left atrium (LA) access, through a steerable 15 Fr sheath (FlexCath Advance, Medtronic), an inner lumen mapping catheter (MC; Achieve, Medtronic) was advanced in each PV ostium. A 28-mm CB-Adv (Arctic Front Advance, Medtronic) was advanced inflated and positioned in each PV ostium. Optimal vessel occlusion was considered as achieved when selective contrast injection showed total contrast retention. Once occlusion was documented, cryoenergy applications were started, lasting at least 180 s. During ablation, if PV potentials (PVPs) were visible, time to isolation was recorded when PVPs completely disappeared or were dissociated from LA activity. Through a single transseptal puncture, an inner-lumen mapping catheter (Achieve®, Medtronic©) was advanced to each PV ostium through a steerable 15 Fr sheath (FlexCath Advance®, Medtronic©, Minneapolis, MN, USA). Baseline electrical information was gathered in each PV ostium. A 28-mm CB-A (Arctic

Front Advance™, Medtronic©) was advanced, inflated, and positioned at each PV ostium. Optimal vessel occlusion was defined by selective contrast injection showing total contrast retention with no backflow into the left atrium. The ablation sequence was treating the left superior PV (LSPV) first, followed by the left inferior PV (LIPV), right inferior PV (RIPV), and right superior PV (RSPV). Once vessel occlusion was deemed satisfactory, delivery of cryoenergy to allow freezing was commenced. Standard cryothermal applications lasted 180 s. Our target temperature was − 40 °C within the first 60 s. If the temperature did not attain this value, an extra freeze was delivered. Successful PVI was defined as an absence of all PV potentials or their dissociation from an atrial activity. During the entire procedure, activated clotting time was maintained over 250 s by supplementing heparin infusion as required.

Isolation was assessed at least 20 min after application. In order to avoid phrenic nerve palsy (PNP), diaphragmatic stimulation was achieved by pacing the phrenic nerve during septal PV ablation.

2.5 Repeat procedures

Through a single transseptal puncture, an inner-lumen mapping catheter (Achieve®, Medtronic©) was advanced to each PV ostium through a steerable 15 Fr sheath (FlexCath Advance®, Medtronic©, Minneapolis, MN, USA). Baseline electrical information was gathered in each PV ostium. A 28-mm CB-A (Arctic Front AdvanceTM, Medtronic©) was advanced, inflated, and positioned at each PV ostium. An initial re-PVI was performed if necessary with the CB-A. Subsequently, ablation of the LAPW was performed in all patients. Standard cryothermal lesions lasted 180 s. Cryoenergy applications were interrupted in case of recorded inner oesophageal temperatures of 15 °C or less. In order to achieve the later, the achieve catheter was placed deeply in the LSPV to stabilize the cryoballoon, with the distal balloon freezing surface oriented towards the LAPW. The first cryoenergy application was performed close to the balloon position during isolation of the LSPV to generate continues lesions at the LAPW. By a slight clockwise rotation and progressive "pullback" of the sheath while keeping the cryoballoon in contact with the posterior wall, consecutive freezes were applied along the LAPW in an overlapping manner, until the original balloon position for isolation of the RSPV was reached. For the most rightwards applications the balloon was slightly retracted if necessary in order to reach the vicinity of the RSPV ostium. The same maneuver was performed between the LIPV and RIPV with the finality of accomplishing complete LAPWI. After the completion of the LAPW ablation, an electrical external cardioversion was performed if AF persisted. At the end of the procedure, in order to evaluate LAPWI pacing, maneuvers to test entrance and exit block were performed by placing the achieve catheter (Medtronic, Minneapolis, USA) on the posterior wall in sinus rhythm. Also, a high-density 3D electroanatomical map (CARTO 3, Biosense Webster) was created with a multielectrode mapping catheter (Pentaray, Biosense Webster, USA). Areas of low voltage were defined as < 0.15 mV.

2.5.1 Assessment of esophageal temperature

The CIRCA's S-CATH™ Esophageal Temperature Monitoring System (Biotronik) was used for every procedure. The S-CATH deploys an array of 12 temperature sensors throughout the length and width of the esophagus, positioning sensors near the source of temperature changes. The CIRCA system incorporates a monitor that displays the data from all 12 sensors. If required, the location of the esophageal probe was modified to the suitable position according to the CB-A position during freezing for a precise measurement of the LET, under fluoroscopic guidance.

2.6 Postprocedural management

After the procedure, patients were continuously monitored via telemetry for at least 18 h. Before discharge, a TTE was performed in all patients in order to exclude postprocedural complications. Oral anti-coagulation was resumed on the evening after the procedure and continued for a minimum of 3 months. After discharge, patients were scheduled for follow-up visits with baseline ECG and 24 h Holter recordings at 1, 3, 6, and 12 months and thereafter every 6 months. Additional Holter recordings and clinical evaluation were performed if deemed necessary in the case of symptoms suggesting arrhythmic recurrence.

2.7 Statistical analysis

Patient information was retrospectively entered into a computed database. Continuous variables are expressed as mean ± SD. Categorical variables are presented as absolute numbers and percentages.

3 Results

3.1 Baseline characteristics

A total of 33 patients underwent a repeat ablation procedure due to recurrence of documented AF following an initial CB procedure for persistent AF. Mean duration of AF prior to index procedure was 17 ± 12 months and mean LA diameter at the index procedure was 43 ± 8 mm. Mean time to recurrence of AF was 8.09 ± 2.64 months prior to the repeat procedure. All patients recurred with PersAF before the repeat

procedure. Mean duration of persistence of index AF episode immediately before the redo procedure: 4.4 ± 2.1 months Specific baseline characteristics are listed in Table 1.

3.2 Index procedure characteristics

All procedures were carried out with the large 28 mm diameter second-generation CB. Mean procedural duration was 66 ± 20.1 min. Mean fluoroscopy time was 13.9 ± 6.6. Mean minimal temperature was − 49.0 ± 5.6 °C in the LSPV, − 48.0 ± 5.8 in the LIPV, − 51.8 ± 5.3 °C in the RSPV, and − 48.9 ± 5.6 °C in the RIPV. No major complications occurred during the index procedure (Table 2).

3.3 Repeat procedure characteristics

Mean procedural time was 75 ± 12 min. Mean fluoroscopy time was 13 ± 5 min. All patients presented in AF at the beginning of the procedure. Atrial fibrillation terminated in three patients (9%) during posterior wall ablation. Re-isolation of reconnected PVs did not lead to AF termination in any patient (Table 3).

3.3.1 Pulmonary vein reconnection

Electrical reconnection could be documented in 18 veins (13%). Specifically, reconnection was observed in five LSPV (27%), four LIPV (22%), five RSPV (27%), and four RIPV (22%). Re-isolation was achieved with a single freeze in all veins and persisted during the whole duration of the procedure.

3.3.2 Left atrial posterior wall isolation

The LAPW was successfully isolated solely by CB-A ablation in 30 out of 33 (91%) patients; in the remaining 3 patients, isolation of the LAPW was completed by focal tip-irrigated RF ablation. The mean number of CB-A applications required for the superior portion of the LAPW and the inferior portion of the LAPW creation were 5.4 ± 0.9 and 4 ± 0.6, respectively. Mean duration of single cryoenergy application on the posterior wall was 178 ± 8 s; average time required to achieve ablation of the superior portion of the LAPW was 16.41 ± 1.3 and 12.1 ± 1.3 min for the inferior portion. Focal tip radio-frequency applications were performed in the midregion of the inferior portion due to failure of maintaining the CB in a stable position during the cryoenergy application.

Interruption of the application due to a LET below 15 °C occurred in four patients (12%), two at the LIPV and two in the superior portion of the LAPW. Complete LAPWI could be observed in all four patients.

Table 1 Baseline characteristics of the population

Baseline characteristics	
Age	56.70 ± 12.03
Female	12 (37.5%)
Coronary artery disease	2 (6.3%)
Diabetes	4 (12.5%)
Hypertension	14 (43.8%)
LVEF	57.58 ± 6.07
LA volume	42.84 ± 8.35
PV anatomy	
Normal	27 (84.4%)
Left common Os	2 (6.3%)
Early branching	2 (6.3%)

Table 2 Index procedure characteristics

Index procedure characteristics	
Fluoroscopy time	13.91 ± 6.32
Procedure time	66.00 ± 20.12
Minimal temp LIPV	− 48.53 ± 4.23
Minimal temp LSPV	− 49.91 ± 5.05
Minimal temp RIPV	− 48.03 ± 3.69
Minimal temp RSPV	− 49.66 ± 3.87
Temp 60 s LIPV	− 41.53 ± 3.10
Temp 60 s LSPV	− 41.09 ± 4.19
Temp 60 s RIPV	− 40.25 ± 5.30
Temp 60 s RSPV	− 38.93 ± 15.34
Temp at isolation LIPV	− 29.65 ± 7.83
Temp at isolation LSPV	− 33.88 ± 7.75
Temp at isolation RIPV	− 30.12 ± 9.80
Temp at isolation RSPV	− 27.39 ± 9.44
Time to isolation LIPV	38.83 ± 21.70
Time to isolation LSPV	41.08 ± 9.41
Time to isolation RIPV	37.35 ± 20.49
Time to isolation RSPV	25.89 ± 10.33

LSPV, left superior pulmonary vein; *LIPV*, left inferior pulmonary vein; *RIPV*, right inferior pulmonary vein; *RSPV*, right superior pulmonary vein

3.4 Follow-up

The mean follow-up was 11.8 ± 3 months. Twenty-eight patients (85%) did not experience recurrence of any atrial arrhythmias during follow-up, without the need of further ablation or class I or III AADs. Of the five patients (15%) that had recurrence of atrial tachyarrhythmia, three presented with PersAF (9%) and two with typical atrial flutter (6%). Both patients with atrial flutter underwent successful cavotricuspid isthmus ablation without recurrence of any arrhythmia in the follow-up. All three patients recurring with PersAF underwent ECV and were put on AAD treatment by the referring

Table 3 Repeat procedure characteristics

Repeat procedural characteristics	
Procedure time redo	75.78 ± 12.06
Follow-up after redo	11.78 ± 3.06
TTR after index	4.50 ± 2.94
Time from index to redo	8.09 ± 2.64
Reconnection LIPV	4 (12.5%)
Reconnection LSPV	5 (15.6%)
Reconnection RIPV	4 (12.5%)
Reconnection RSPV	5 (15.6%)
Min LET lower	− 31.09 ± 5.92
Min LET upper	− 31.38 ± 6.29
Min temp lower	− 41.78 ± 4.63
Min temp upper	− 41.66 ± 4.80
N of applications roof	
3	5 (15.63%)
4	10 (31.25%)
5	14 (43.75%)
6	3 (9.38%)
N of applications bottom	
2	1 (3.13%)
3	15 (46.88%)
4	15 (46.88%)
5	1 (3.13%)
Need for RF "touch-up" in PB	3 (9%)

TTR, time to recurrence; *LET*, luminal esophageal temperature; *LSPV*, left superior pulmonary vein; *LIPV*, left inferior pulmonary vein; *RIPV*, right inferior pulmonary vein; *RSPV*, right superior pulmonary vein; *PB*, posterior box

cardiologist without undergoing any other interventional procedure.

3.5 Procedural complications

One transient phrenic nerve palsy (3%) occurred during cryoenergy application in an RSPV. The diaphragmatic contraction readily resumed shortly after the interruption of the freeze.

4 Discussion

The main findings of the current study is that a strategy based on isolating the posterior wall of the LA with the CB-A is feasible in most cases and offers freedom from Af in 85% of patients undergoing a repeat procedure for recurrent PersAF.

The optimal ablation strategy in the setting of PersAF is still a matter of debate. While the STAR AF 2 trial [12] reported that creating additional lines or eliminating CAFE potentials in adjunction to PVI did not offer any advantage, others report very satisfactory outcomes following substrate modification during AF ablation in this patient population [13, 14].

The posterior LA wall can show structural abnormalities in PersAF. These usually consist in conduction abnormalities, higher incidence of delayed after depolarizations, and larger late sodium and intracellular and sarcoplasmic reticulum Ca21 contents but smaller inward rectifier potassium currents [15–18].

Therefore, this portion of the atrium is believed to be crucial in sustaining atrial fibrillation. With these considerations in mind, many authors have described the beneficial consequences of targeting the posterior wall as a part of an ablation lesion set. Although, most articles regarding this strategy reported outcomes with RF energy, off late a few studies focusing on LAPWI with the CB-A have been published [10, 11]. In an interesting report, Kuniss reported on the creation of a roof line and its beneficial effect on the treatment of PersAF [11]. Much to their surprise, electroanatomical maps following ablation showed that the lesion extended well beyond the roof and comprised a large portion of the posterior wall. Outcomes were, as expected, better than PVI only. In fact, nearly 80% of individuals did not present AF relapse on a midterm follow-up of 12 months. Similarly, Aryana et al. elegantly described the clinical outcome of LAPWI in a multicenter trial. This time, the authors purposely created a posterior wall isolation with the CBA by both creating superior and inferior lines between PVs following successful PVI. In addition, Aryana et al. compared this cohort with a similar series of patients presenting PersAF but treated by PVI only. Not surprisingly, patients having undergone PVI+ LAPWI did significantly better [10].

Despite these promising results, in a non-negligible proportion of patients affected by persistent AF, the index ablation strategy still consists in PVI only in many EP laboratories worldwide. As mentioned above, this might be due to the lack of a standardized ablation strategy beyond PVI in patients affected by persistent AF. Importantly, while Aryana et al.'s patient population consisted in ablation-naive individuals undergoing PVI+ LAPWI as an index procedure for persistent AF, our study focused on patients undergoing LAPWI as a repeat procedure due to AF recurrence after an initial PVI with the CB. Our findings suggest that LAPWI in this particular cohort might be beneficial and might therefore be advised to operators who choose to perform only PVI with the CB during an index procedure for persistent AF.

In our study, the creation of a posterior box proved to be feasible and safe in our study. Interestingly, despite targeting the posterior wall, LET did not reach low temperatures in most patients. This might be due to the "sitting" position of the balloon on the posterior wall while ablating. This probably results in a distribution of the lesion on a wider surface therefore reducing the pressure on a specific point. However,

although the occurrence of atrioesophageal fistula is rare during CB ablation, the operator should not underestimate this risk when targeting the posterior wall and should imperatively stop the freeze if a low temperature in the esophagus would be recorded. In addition, patients should be instructed to immediately report to their physician sudden fever, chest pain or neurological symptoms appearing in the days or weeks after the procedure.

This strategy guaranteed freedom from any atrial arrhythmia in most patients at 12 months follow-up. This finding confirms the crucial role played by the posterior wall in sustaining AF. Due to the proximal extension of the lesion to a large portion of the PV antrum [19], completing LAPWI might not be as cumbersome. In fact, with a mean total number of 9 ± 3 applications, the posterior wall could be isolated solely with the balloon in 91% of patients.

4.1 Study limitations

The present study carry the limitation of being single-center and non-randomized study. Future larger studies with longer follow-up are needed to confirm these data. No systematical esophagogastroduodenoscopy was performed, thus underestimating the incidence of esophageal lesions. There was no comparison with a group in which only re-isolation of PVs was performed. Therefore, the impact of the redo isolation of the PVs on clinical outcome could have played an important role in keeping patients in sinus rhythm. Furthermore, no pharmacological protocol to elicit non-PV triggers was performed.

5 Conclusions

Left posterior wall isolation with the CB-A is feasible and safe during repeat ablation procedures for recurrent PersAF. In our study, the 12-month freedom from any arrhythmia was 85% following this ablation strategy.

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