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ORIGINAL PAPER

A novel double cryoballoon strategy in persistent atrial fibrillation: a pilot study

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Abstract
Aims Cryoballoon technology is a promising technique in paroxysmal atrial fibrillation (AF) ablation. However, success rates in patients with persistent AF have not been convincing. There is a trend toward performing more extensive procedures that are referred to as 'pulmonary vein isolation plus.' To combine pulmonary vein isolation (PVI) and antral substrate modification, we used both the 23-mm and 28-mm cryoballoon in a single approach in patients with persistent AF.
Methods and results 33 consecutive patients (26 men, age 60 ± 10 years, LA size 44 ± 5 mm) with persistent AF were prospectively included. All patients underwent the "double balloon strategy:" at least two applications at each pulmonary vein (PV) using the smaller 23-mm balloon to isolate the PV at the ostial level plus at least one additional freeze by the 28-mm balloon at the wide PV antral level. 7-day Holter monitors were performed during follow-up at 1, 3, 6, 9, 12, 18 and 24 months post-ablation. 131 of 133 PVs were targeted and isolated (98.4 %). A mean of 14 ± 2 cryoballoon applications per patient or 3.5 ± 1.5 applications per vein were performed. After a single procedure and mean follow-up of 15 ± 3 months, 69.7 % of patients remained in sinus rhythm (3-month blanking period). There were no major complications.
Conclusions In persistent AF, the "double balloon strategy;" combining the small and large cryoballoon allowed ostial PV isolation followed by antral cryoablation is feasible, safe and associated with a favorable outcome.

Keywords Catheter ablation · Persistent atrial fibrillation · Cryoballoon · Double balloon strategy

List of abbreviations

AF	Atrial fibrillation
PV	Pulmonary vein
PVI	Pulmonary vein isolation
LA	Left atrium
LSPV	Left superior pulmonary vein
LIPV	Left inferior pulmonary vein
RSPV	Right superior pulmonary vein
RIPV	Right inferior pulmonary vein
SD	Standard deviation
ICE	Intracardiac echocardiography
PNP	Phrenic nerve palsy

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Introduction

Catheter ablation is extensively used in the treatment of atrial fibrillation (AF) with curative intention. Cryoballoon technology (Arctic Front, Medtronic, USA) has emerged as a promising and safe approach to pulmonary vein isolation (PVI) in short and longterm follow-up of paroxysmal AF patients [1–5]. Two different sizes of the cryoballoon are

currently available. A smaller (23 mm) and a larger (28 mm) balloon relative to the ostial diameter of the pulmonary veins (PV). A complete occlusion of the PV is key for PVI success. The largest trial was published by Neumann et al. [3] including 293 patients with paroxysmal AF and a success rate of 74 % of maintained sinus rhythm. However, in 53 patients with persistent AF, freedom from AF was observed in only 42 %. A similarly limited success rate of 48 % was reported recently in 34 patients with persistent AF [5].

Although ablation techniques and strategies vary among centers, there is a general trend favoring PVI alone for treatment of paroxysmal AF and PVI combined with left atrial substrate modification for treatment of persistent AF [6–8]. In persistent AF, more extensive procedures are performed which can be broadly referred to as 'PV isolation plus.'

To induce substrate modification beyond PVI only at the ostial level of the PVs, we combined the use of both the 23 and 28-mm cryoballoon in one single approach in patients with persistent AF. The strategy was to combine cryoballoon induced ostial and wide antral lesions in each individual PV of the patients. We report our pilot study investigating a new "double cryoballoon strategy" approach in patients with persistent atrial fibrillation.

Methods

Patients

Between December 2009 and November 2010, 33 consecutive patients with symptomatic persistent AF were included in the prospective study. Persistent AF was defined as episodes of AF that lasted >7 days without intervention [9]. All patients underwent their first AF ablation procedure. In all study subjects, cryoballoon PVI using the "double balloon strategy" was performed at our institution.

Exclusion criteria were as follows: age <18 years or >80 years, repeat procedure for recurrent AF, ejection fraction <30 %, left atrial size >55 mm, left atrial thrombus, inability to consent and life expectancy <1 year.

All patients gave written informed consent prior to inclusion in the study. The local institutional ethics committee approved the study.

Ablation protocol

All PVI procedures were performed under conscious sedation and analgesia with appropriate doses of fentanyl and midazolam. A decapolar catheter was placed into the coronary sinus. After venous and arterial access for real-time blood pressure monitoring, a single transseptal puncture was performed under guidance of intracardiac ultrasound (ICE) using a modified Brockenbrough technique to introduce an 8-F sheath (St. Jude Medical, USA) and the steerable 12-F sheath for cryoballoon (FlexCath, Medtronic, USA) introduction. After transseptal puncture an infusion of heparin was maintained to achieve an activated clotting time of 300–400 s during the LA procedure. Activated clotting time measurements were performed every 30 min routinely. Pulmonary vein potentials were checked at least before and after PV isolation with a circular mapping catheter. To record the PV potentials during the cryoballoon freezes an 8-pole circular mapping catheter (Achieve, Medtronic, USA) was used which was introduced into the central lumen of the cryoballoon catheter.

If AF was present direct current cardioversion was performed to restore sinus rhythm prior to ablation start. To assess the exact position of the inflated balloon relative to the PV ostium, contrast agent (dye diluted in 1:1 ratio with 0.9 % saline) was injected from the distal lumen of the cryoballoon to obtain a PV angiogram. Cryoballoon occlusion of the vein was quantified according to a semi-quantitative grading method described earlier (from grade 4 = excellent: full retention of contrast medium without outflow in the LA down to grade 1 = very poor with an immediate outflow from the vein) [3].

Cryoballoon ablation: double balloon strategy

To combine ostial PV isolation and wider PV antral lesions, both balloons were used in a single procedure (Fig. 1). First, the smaller balloon was introduced. At least two applications (300 s per freeze) using the 23-mm balloon at the PV ostial level were performed. For freezes of the RSPV the small balloon was not used if the maximum diameter of the PV exceeded 21 mm to minimize the risk of phrenic nerve injury. PV isolation (defined as PV entrance block with complete loss of all PV signals) was confirmed by the 8-pole circular mapping catheter. After PV isolation was achieved one safety freeze was performed. Local temperature in the PV antrum was continuously monitored from a temperature sensor at the proximal part of the cryoballoon. If complete PV isolation was confirmed by the circular mapping catheter the bigger 28-mm cryoballoon was introduced and at least one additional freeze at the wide PV antral level was added. Using the double balloon strategy all individual PVs were treated as described including left common os and additional right middle PV if present.

At the end of the procedure the electrophysiological end point of entrance block was reconfirmed using the circular mapping catheter for each PV.

If typical atrial flutter had been previously documented during electrocardiographic monitoring, cavotricuspid

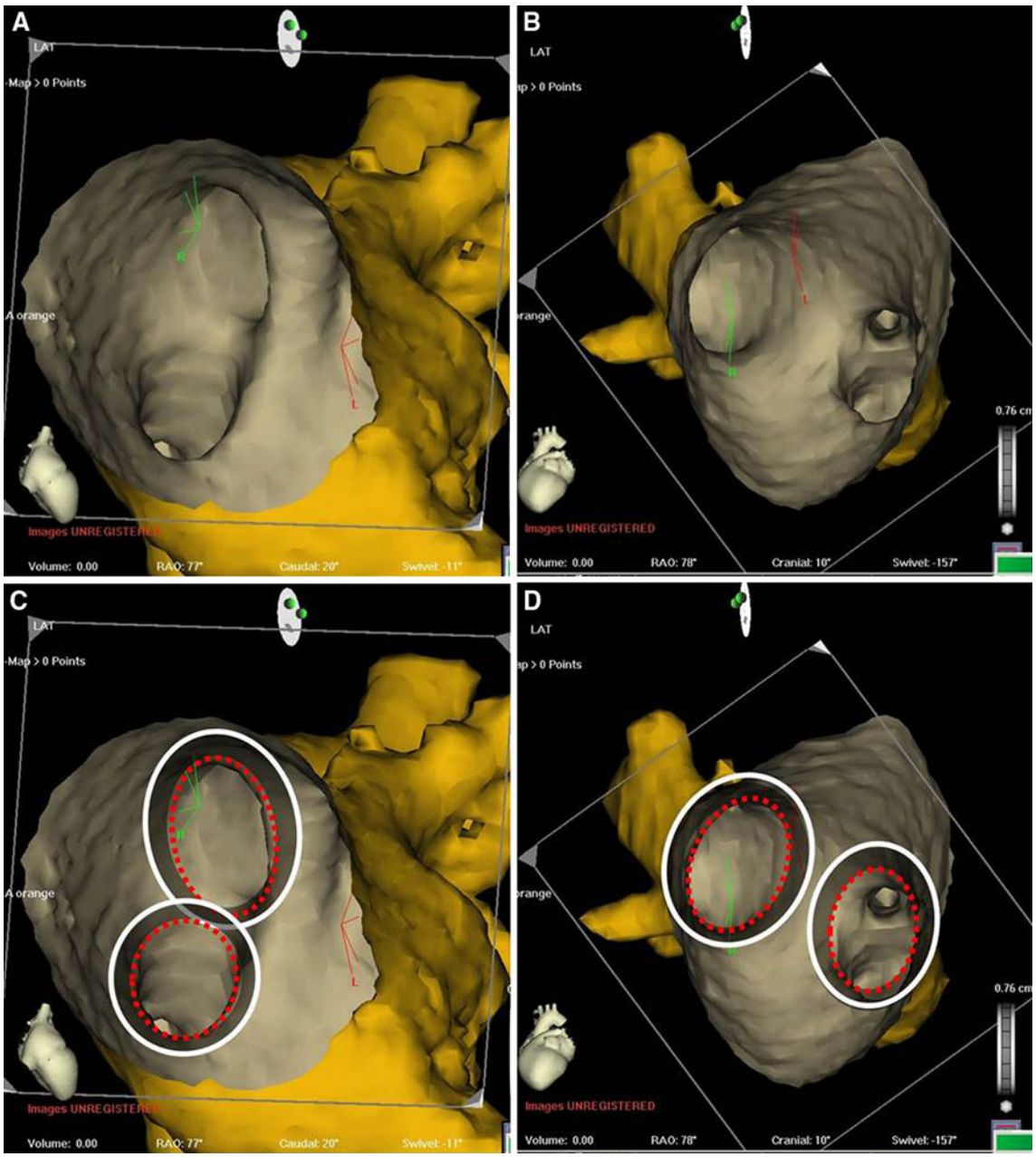

Fig. 1 **a**–**d** Double cryoballoon strategy—the schematic drawings illustrate Carto Merge clipping plane views from preprocedural three-dimensional reconstructed CT scans. **a** and **c** left-sided PV ostia in RAO 77°, caudal 20° view, **b** and **d** right-sided PV ostia in RAO 78°, cranial 10° view. In **c** and **d** characteristic lesion formation related to cryoballoon size are shown: *red dotted line* 23-mm cryoballoon lesion, *white solid line* 28-mm cryoballoon lesion

isthmus ablation was performed using an 8-mm tipped radiofrequency catheter (Gold-tip Flex cathether, Biotronik, Germany) (70W, 60C) until bidirectional isthmus block was achieved.

Peri-operative safety care

The day prior to the procedure, transthoracic echocardiography to assess LA diameter and left ventricular ejection fraction and transesophageal echocardiography was performed, to rule out LA thrombus formation. A CT scan was performed prior to the ablation procedure in all patients. After segmentation of the left atrium, the left atrial volume and pulmonary vein diameters were analyzed.

Phrenic nerve monitoring: A deflectable quadripolar catheter was introduced via the left femoral vein for pacing in the superior vena cava to capture the right phrenic nerve. Continuous monitoring of the phrenic nerve during

ablation of the right superior and inferior PV either was performed in all patients to reduce the risk of phrenic nerve palsy (PNP). Cryoballoon applications were immediately terminated in case of any attenuation of the strength of right hemidiaphragmatic contractions.

Anticoagulation: In patients receiving oral anticoagulants, warfarin was stopped 5 days prior to the procedure with bridging tinzaparin (175 IU/kg). Post-ablation all patients were heparinized with tinzaparin 175 IU/kg until oral anticoagulation with phenprocoumon with a target INR of 2.0–3.0 for at least 3 months was reassumed.

Intracardiac echocardiography guidance of the procedure

All freezes and navigation of the cryoballoon catheter were monitored by the use of ICE (AcuNav, Siemens Medical Solution, Germany). The catheter was introduced through an 11-Fr sheath via the left femoral vein and positioned, fluoroscopically guided, into the right atrium. The electrophysiologist then optimized the ICE images. The position of the cryoballoon at the ostial and antral level of the PV was demonstrated. The whole antrum was visualized to optimize Doppler alignment for each PV during freezing. The optimal position of the cryoballoon in relation to the ostial and antral level of the PV was assessed utilizing ICE, visualized as a full occlusion of the PV with documented loss of Doppler coded reflow to the left atrium and angiography (PV angiogram occlusion grade 4).

Post-ablation management and follow-up

Pericardial effusion and pulmonary infiltration were ruled out in all patients with a transthoracic echocardiography and a chest X-ray following ablation. A 24-h Holter ECG was performed in all patients between day 1 and day 3 post-ablation. Antiarrhythmic drugs were continued 3 months after the procedure to facilitate maintenance of sinus rhythm. At 3 months antiarrhythmics were stopped or continued according to the clinical follow-up and the discretion of the treating electrophysiologist.

During follow-up, all patients were advised to contact us at any time in case of palpitations for ECG registration. They were prospectively followed and underwent an outpatient visit at 1, 3, 6, 9, 12, 18 and 24 months post-ablation. Follow-up included clinical examination, ECG, transthoracic echocardiography and 7-day Holter ECG monitoring to detect recurrence of AF. An event recorder was applied in case of rare palpitations without ECG documentation. Recurrent AF was defined as any symptomatic or asymptomatic detected episode lasting >30 s [9].

Endpoint

The primary endpoint of the study was freedom from AF recurrence. Procedure-related complications was the secondary endpoint.

Statistical analysis

Continuous variables are reported as mean ± standard deviation (SD) or median. Categorical variables are reported as numbers and percentages. Continuous variables were analyzed for a normal distribution using the Kolmogorov–Smirnov test. Comparison of continuous variables was performed using the Student's t test.

Event-free survival was calculated according to the Kaplan–Meier method, with time of first recurrence of atrial fibrillation as the outcome variable including a blanking period of 3 months $p < 0.05$ considered significant.

Analysis was performed using the Statistical Package for the Social Sciences (version 19.0, SPSS, Inc., Chicago, USA). The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the written manuscript.

Results

Patients

Patient characteristics are presented in Table 1. 33 consecutive patients (26 men; mean age 60 ± 11 years) with persistent AF were included in the study. Mean AF history prior to ablation was 51 ± 40 months (range 4–132 months) and the mean duration of the last persistent AF episode was

Table 1 Baseline patient characteristics

Variable	Patients ($n = 33$)
Male gender	26/33 (78 %)
Age (years)	60 ± 11
History of AF (months); median (range)	52 ± 40; 36 (4–132)
Duration of AF (days); median (range)	109 ± 112; 31 (9–744)
Prior cardiac surgery	1/33 (3 %)
Hypertension	17/33 (52 %)
Coronary artery disease	10/33 (26 %)
Dilative cardiomyopathy	2/33 (6 %)
Ejection fraction (%)	58 ± 10
Left atrial size 2D echocardiography (mm)	44 ± 6
Left atrial volume 3D CT angiography (ml)	151 ± 38
Prior ineffective antiarrhythmic drugs	2 ± 1
Amiodarone prior to ablation	18/33 (55 %)

109 ± 112 days (median: 31 days; range 9–744 days) prior to PV ablation. Antiarrhythmic therapy had failed using a mean number of 2 ± 1 antiarrhythmic drugs (AAD). Mean left atrial diameter by echocardiographic parasternal long axis view was 44 ± 6 mm. Typical PV anatomy consisting of 4 distinct PV were found on preprocedural segmentation of CT scans in 28 patients. Two patients had a left common os, an additional right middle PV was found in three patients. The size determined as the maximum diameter of the PVs was as follows:

LSPV: mean 19.8 ± 2.7 mm, median 19 mm, range (15–24 mm), LIPV: mean 20.9 ± 4 mm, median 20 mm, range (13.6–29.6 mm), RIPV: mean 19.8 ± 3.2 mm, median 19 mm, range (13–28 mm) and RSPV: mean 21.7.8 ± 2.6 mm, median 22 mm, range (16.9–26 mm).

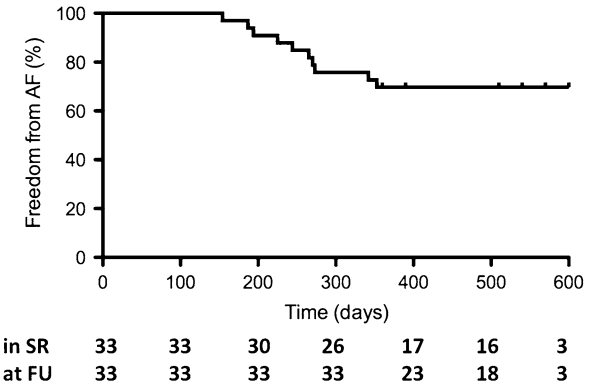

Fig. 2 Kaplan–Meier curve of electrocardiogram-documented persistent atrial fibrillation-free survival after pulmonary vein isolation with a blanking period of 3 months. Patients (*Pts.*), sinus rhythm (*SR*), and follow-up (*FU*)

Acute procedural results

In 33 patients, a total of 133 PVs including 2 with left common ostia were identified and treated. 131 of the 133 PVs (98.4 %) were electrically isolated using the cryoballoon technique exclusively. No PV reconduction was observed until the end of the procedure.

Procedural data

The mean procedural duration was 209 ± 53 min. The mean fluoroscopy time was 48 ± 11 min resulting in a mean dose area product of 5754 ± 3536 cGy. The mean volume of contrast medium used was 157 ± 55 ml.

A mean of 14 ± 2 cryoballoon freezes were applied per patient. Mean number of balloon applications per vein was 3.5 ± 1.5. Minimum cryoballoon temperatures (local temperature at the proximal part of the cryoballoon) during freezing were −75 ± 7 for LSPV, −76 ± 10 for LIPV, −69 ± 7 for RSPV and −72 ± 9 for RIPV using the 23 mm balloon and −50 ± 7 for LSPV, −45 ± 11 for LIPV, −49 ± 7 for RSPV and −52 ± 9 for RIPV utilizing the 28 mm balloon. Radiofrequency cavotricuspid isthmus block was successfully performed in one patient.

Follow-up and AF recurrence

All patients were discharged in sinus rhythm. 7-day Holter ECG monitoring was performed for a median of 15 months (range 12–26 months) post-ablation. At least 12 months of follow-up was completed by all patients. Stable sinus rhythm as the primary endpoint was documented throughout the follow-up period in 23/33 patients (69.7 %, 3-month blanking period, Fig. 2) and in 21/33 patients (63.6 %, without blanking period). Antiarrhythmic drugs were discontinued in 17 patients (52 %) 3 months and in 28 patients (85 %) 6 months post-AF ablation. No organized atrial tachycardias were detected during follow-up, with AF being the only recurrent arrhythmia. A repeat procedure was performed in three patients with symptomatic AF recurrence within 12 months after the index ablation. In all repeat procedures the "double balloon strategy" was performed as described above with respect to PV reconnection confirmed by remapping the PVs during the redo procedure.

Predictors of AF recurrence

Screening for predictors of AF recurrence included age, hypertension, coronary artery disease, left atrial diameter, ejection fraction, use of antiarrhythmics, trough balloon temperature and grading of PV occlusion (dye contrast reflow in LA). Hypertension was the only predictor for AF recurrence (Table 2).

Procedural complications

There were no major periprocedural complications including thromboembolic events, PV stenoses or tamponades observed in our patients. One minor complication occurred in 33 patients (3 %). One patient suffered from an aneurysma spurium the day after ablation which could be successfully treated by manual compression.

In one patient a freeze using the 28-mm cryoballoon at the RSPV was immediately terminated when phrenic nerve capture was lost. Phrenic nerve function recovered completely within 2 min after the freeze was terminated. The ratio of PV size (maximum diameter 26 mm) to balloon size (28 mm) was 0.93. According to our protocol a 23-mm balloon had not been used to treat this PV.

Table 2 Screening for potential predictors for recurrence of atrial fibrillation (≥6-months follow-up)

	No AF recurrence $n = 23$	AF recurrence $n = 10$	p value (<0.05)
LA diameter (mm)	45 ± 6	43 ± 7	$p = 0.28$
Ejection fraction (%)	54 ± 10	51 ± 1	$p = 0.50$
Coronary artery disease	7/23 (31 %)	3/10 (30 %)	$p = 0.39$
Hypertension	9/23 (39 %)	8/10 (80 %)	$p = 0.02$
AF history (months)	47 ± 49	52 ± 43	$p = 0.65$
Time to PVI (s)	49 ± 36	51 ± 44	$p = 0.51$
Trough ballon temperature (°C)	55 ± 12	60 ± 8	$p = 0.15$
Grading of PV occlusion	3.8 ± 0.1	3.9 ± 0.1	$p = 0.25$

LA left atrium, *AF* atrial fibrillation, *PVI* pulmonary vein isolation

Discussion

Ablative treatment of persistent AF with curative intention remains challenging. For the first time, the present study reports on a novel "double cryoballoon strategy" utilizing both the smaller 23-mm and the larger 28-mm cryoballoon in a single ablation procedure. Our study demonstrates this strategy can be performed safely and effectively with a success rate of 69.7 % freedom from AF after follow-up of 15 ± 3 months in patients with persistent atrial fibrillation. Furthermore, although both cryoballoon sizes were used in a single procedure the complication rate was rather low without major complications.

Previous data and role of atrial substrate in persistent AF

Published outcome data in AF ablation show variable results related to the ablation method used, patient selection and follow-up. A recent review of the literature revealed an efficacy of 60–80 % freedom from AF at 12 months follow-up with a single AF ablation procedure in well selected patients with paroxysmal AF. In persistent (50–70 %) and longstanding persistent (below 50 %) AF patients, efficacy rates are not optimal [5, 7, 10]. While the endpoint of PVI is the agreed goal in paroxysmal AF [9], the targets and endpoints of ablation for persistent AF are not well defined yet [11].

Considerable experimental and clinical evidence suggests that as AF progresses from paroxysmal to persistent, the atrial substrate becomes increasingly abnormal and may play a more important role in maintaining the arrhythmia [12–17].

Since the modification of the left atrial substrate seems to play an important part, there is a trend for more extensive procedures ('PV isolation plus') in radiofrequency (RF) ablation of persistent AF. Ablation lesions have migrated more proximally to 'encircle' the pulmonary vein antra, in order to enclose a larger region of posterior left atrial myocardium. Current strategies are based on achieving PVI prior to targeting left atrial substrate modification including ablation of complex fractionated electrograms, the creation of linear lesions, or both [8, 18, 19]. However, concerns have been raised that more extensive ablation may increase the risk of complications and impair left atrial mechanical properties [20–22].

In previous reports cryoballoon therapy had limited success in persistent AF patients (3–5). It was shown that PVI may not be sufficiently achieved in all pulmonary veins using a single size cryoballoon. Although it is well known that focal cryoablation catheters have limitations regarding their use in AF ablation therapy they had to be additionally used to complete PVI after insufficient single cryoballoon therapy [2, 4, 23]. Since PVI is the cornerstone in any AF ablation procedure a single cryoballoon size may not be sufficient, certainly in persistent AF patients.

It was presumed that the strategy of the cryoballoon device might not produce sufficient substrate modification as required in persistent AF [3]. In two separate series, detailed electroanatomical mapping was used before and after cryoballoon applications to determine the anatomical level at which PV isolation was achieved. When the 23-mm balloon was used, the PVs were found to be isolated at the ostial level, whereas use of the 28-mm larger balloon results in the formation of much wider, circumferential and antrally located lesions. Another trial revealed that the extent of PVI significantly differed when the lesions with either balloon sizes were compared. The lesion created with the 28-mm balloon included a larger portion of the left atrium. Using the 23-mm balloon the mean documented extent of electrical isolation was 20.7 ± 2.8 % of the maps' surface, compared to 40.2 ± 3.9 % when performing ablation with the 28-mm balloon [24–26].

Mansour et al. [27] reported a combined approach using a cryoballoon for PVI and focal RF ablation to induce left atrial substrate modification in 22 persistent AF patients with promising procedural and short-term follow-up results in terms of efficacy and safety. However, the combination of cryo- and RF energy performed in a single approach in the left atrium means increased radiation and is time

consuming and needs to be confirmed and approved in larger trials also with respect to safety and the patient periprocedural comfort.

Thus, our proposed double balloon approach using both cryoballoon sizes might overcome the limitations of prior single balloon therapies in persistent AF with respect to insufficient PVI in selected PVs due to a mismatch of balloon/diameter size and solely ostial lesion formation using the 23-mm cryoballoon only. Compared to the combined use of cryo- and RF energy our procedure and fluoroscopy times were shorter with promising efficacy and safety rates [27].

Predictors of success in "double balloon strategy" in persistent AF

Successful PVI using the cryoballoon approach requires optimized wall contact within the left atrium encircling the PVs. Incomplete wall contact may result in conduction gaps and prevent complete PVI which was shown primarily for the inferior aspect of the PVs during analysis of redo procedures [28]. Data from Kuck et al. [29] using a single big balloon only demonstrated an acute success rate of >98 % isolated PVs. However, these promising results could not be reproduced in other centers. Andrade et al. [30] found in their review of 23 cryoballoon studies an acute success rate of 92.6 % isolated PVs using the cryoballoon catheter alone without focal ablations. Including focal "touch-up" ablations using cryo or RF energy the acute success rate increased to 98.8 %. We also found a strong acute success rate of 98.4 % with 131 of 133 isolated PVs. Since our acute success rate translated in a freedom from AF of 69.7 % in persistent AF patients at 15 ± 3 months follow-up, this appears to be related to the use of both balloon sizes combining ostial and more antrally located lesions. In most patients' anatomy an optimized wall contact can be achieved more effectively with the 23-mm instead of the 28-mm balloon, but the PV isolation site of the 23-mm balloon would be more distal compared to the PV antrum. However, the PV antrum has been proven important for initiation as well as for maintenance of atrial fibrillation [31, 32]. Even in longstanding persistent AF patients and RF ablation pulmonary vein antrum isolation has been proven an important endpoint in maintaining SR which should be the cornerstone also in any ablation procedure in persistent AF patients [6, 33]. Thus, the combination of an optimized left atrial-PV wall contact more distally using the 23-mm balloon and the additional antral lesion formation using the 28-mm freeze seems to be key in the "double balloon strategy."

In cryoballoon ablation temperature measurement is a less dependable predictor, since the temperature sensor, located proximally inside the balloon, is outside the PV and underestimates the tissue temperature attained during the freeze. The sensor is warmed by blood flow in neighboring PVs. In our patients a lower trough temperature was not associated with AF recurrence, which might be related to the limited numbers of patients included in this pilot study.

The time to PVI recorded by real-time monitoring of PV potentials throughout the freeze using a circular mapping catheter introduced into the central lumen of the cryoballoon catheter was reported as a promising tool. A cut-off value of 83 s to PV isolation was predictive of stable procedural PVI without reconduction [34]. Since time to PVI reflects the accuracy of the isolation of a single vein it was not predictive of AF recurrence in our persistent AF patients undergoing the "double cryoballoon strategy." This might furthermore be related to the additive effect of the antral lesion formation using the 28-mm cryoballoon after PVI was achieved using the 23-mm balloon.

Complications

Our study supports prior data on the safety of cryoballoon therapy in AF. A major concern utilizing the cryoballoon is PNP. One transient PNP was induced using the 28-mm cryoballoon in a right superior PV with full recovery within 120 s after freeze termination. Our experience would support the recommendation to continuously monitor the phrenic nerve function by pacing in the superior vena cava to capture the right phrenic nerve and avoid a distal balloon ablation within the RSPV as discussed earlier [35, 36].

Although PNP is a major limitation of balloon catheters used in AF ablation, cryoballoon therapy has obvious significant potential safety advantages when compared with RF ablation. Certainly complex RF ablation strategies as recommended in patients with persistent AF carry a significant risk for major complications. Major complications were reported in up to 6 % including the risk of PV stenosis, thromboembolic events, tamponades or atrioesophageal fistula, which were not seen in our patients [11].

Limitations

The number of patients included in the study was relatively small. Since this was a pilot study, evaluating the "double balloon strategy" in terms of efficacy and safety in patients with persistent AF for the first time, larger trials are needed to confirm our findings. However, since 7-day Holters were performed in our patients at close intervals up to 24 months the follow-up of our patients was relatively intense. Of course, longterm follow-up will be important to demonstrate that our data will translate into a longterm freedom from AF in patients with persistent AF undergoing a "double balloon strategy" in cryoablation.

We did not find any symptoms suggestive of PV stenosis in our patients during follow-up and did not perform repeat imaging by use of CT scan or cardiac MRI scan to rule out subclinical PV stenosis. However, since all patients were asymptomatic, such a finding would not have changed the post-ablation management during follow-up.

Radiation exposure still is an issue in cryoballoon ablation. We found a mean dose area product of 5754 ± 3536 cGy and a fluoroscopy time 48 ± 11 min which was in line with data from a recent review of published studies in cryoballoon ablation [30]. The reduction of radiation exposure in cryoballoon ablation using alternative imaging modalities has to be addressed in future trials.

Finally, randomized studies evaluating the efficacy and safety of RF versus cryoballoon therapy will be necessary to compare the value of both ablation therapies in patients with persistent AF.

Conclusion

The results of this pilot study demonstrate that the "double balloon strategy" combining cryoballoon induced ostial PV isolation followed by antral cryoablation for treatment of persistent AF is feasible and is associated with a favorable outcome. Only minor transient and reversible complications occurred. A randomized study in a larger cohort of patients is required to assess efficacy and safety of this new approach in persistent AF patients.

Conflict of interest No disclosures relevant to the manuscript have to be declared.

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