



ELSEVIER

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Pulmonary vein isolation in patients with a left common pulmonary vein: Comparison between second-generation cryoballoon and radiofrequency ablation

Masao Yamaguchi (MD)^a, Shinsuke Miyazaki (MD)^{b,*}, Takatsugu Kajiyama (MD)^a, Masahiro Hada (MD)^a, Hiroaki Nakamura (MD)^a, Hitoshi Hachiya (MD)^a, Yoshito Iesaka (MD)^a

^a Cardiovascular Center, Tsuchiura Kyodo Hospital, Tsuchiura, Ibaraki, Japan

^b Department of Cardiovascular Medicine, Fukui University, Fukui, Japan



ARTICLE INFO

Article history:

Received 25 July 2018

Received in revised form 11 October 2018

Accepted 24 October 2018

Available online 21 December 2018

Keywords:

Left common pulmonary vein

Cryoballoon

Pulmonary vein isolation

Atrial fibrillation

Catheter ablation

ABSTRACT

Background: Adaptability of cryoballoons to anatomic pulmonary vein (PV) variations is limited due to the fixed geometrical shape, and use for left common PVs (LCPVs) is controversial. We compared the procedural and clinical outcomes in patients with LCPVs after cryoballoon and radiofrequency ablation, and explored the morphological parameters associated with procedural difficulty in LCPV isolations using cryoballoons.

Methods and results: Eighty-nine consecutive atrial fibrillation patients with LCPVs undergoing PV isolation using either 28-mm second-generation cryoballoons ($n = 30$) or irrigated-tip catheters ($n = 59$) were included. The patient characteristics except for the left atrial diameter ($p = 0.05$) or morphological parameters obtained from cardiac computed tomography were similar between the two groups. The number needed to disconnect the LCPVs (NND) in the cryoballoon-group was ≤ 3 applications in 22 patients, but ≥ 4 in the remaining 8, including 1 requiring touch-up ablation. The PV isolation procedure time was significantly shorter in the cryoballoon-group than radiofrequency-group (43.0 ± 19.5 min vs. 68.2 ± 31.4 min, $p < 0.001$), whereas the single procedure 1-year atrial fibrillation freedom was similar between the groups (74% vs. 67%, $p = 0.73$). A multivariate logistic regression analysis revealed that the ovality index in the cryoballoon-group (odds ratio = 1.474; 95% confidence interval = 1.020–2.128; $p = 0.039$) and orientation difference between the LCPV and lower branch in the frontal plane (odds ratio = 1.071; 95% confidence interval = 1.008–1.137; $p = 0.026$) were independent predictors of an NND ≥ 4 . The incidence of LCPV reconnections was similar between the cryoballoon- and radiofrequency-groups during the second procedure (50.0% vs. 58.3%, $p = 0.73$).

Conclusions: Cryoballoon ablation was similarly as effective as radiofrequency ablation in patients with LCPVs, and morphological evaluations aided in predicting procedural difficulty in LCPV isolations.

© 2018 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.

Introduction

Pulmonary vein isolation (PVI) has become an established therapeutic option for patients with atrial fibrillation (AF) [1,2]. A prospective randomized study showed that cryoballoon (CB) ablation

and radiofrequency (RF) ablation were similarly effective and safe in patients with paroxysmal AF [3,4]. Thus, the selection of the device for achieving a PVI remains at the discretion of the operator. On the contrary, the PV anatomy varies in individual patients and could influence the procedural outcome. In a point-by-point RF ablation, a tailor-made ablation line could be designed according to the PV anatomy, however, the lesion of the CB ablation might be determined by the PV anatomy due to the limited balloon size and configuration. Left common PVs (LCPVs) are the most frequently encountered PV anomaly in AF ablation. The recently introduced second-generation CB (Arctic Front Advance, Medtronic, Minneapolis, MN, USA) has a

* Corresponding author at: Department of Cardiovascular Medicine, Fukui University, 23-3 Shimo-aiduki, Matsuoka, Eihei-cho, Yoshida-gun, Fukui 910-1193, Japan. Tel.: +81 776 61 8800; fax: +81 776 61 8801.

E-mail address: mshinsuke@k3.dion.ne.jp (S. Miyazaki).

high procedural performance [5,6], however, the data on patients with LCPVs are conflicting [7–10]. Moreover, to date, no data comparing the CB and RF ablation in patients with an LCPV are available. In the present study, we sought to (1) compare the procedural and clinical outcomes of the second-generation CB and RF ablation and (2) explore the anatomical factors predicting the procedural difficulty of an LCPV isolation using a 28-mm CB in patients with an LCPV, to identify a better indication of the CB ablation in patients with LCPVs.

Methods

Study population

This retrospective study consisted of 89 consecutive patients with an LCPV and paroxysmal or short-lasting persistent AF (duration of <3 months) who underwent their first PVI with either a second-generation CB ($n = 30$) or RF ablation ($n = 59$) between June 2012 and July 2017. The ablation system was selected according to the operator's preference after July 2014, and all were performed with RF catheters before July 2014. AF was classified according to the latest guidelines [2]. All patients gave their written informed consent. The study protocol was approved by the hospital's institutional review board. The study complied with the Declaration of Helsinki.

Mapping and ablation protocol

All antiarrhythmic drugs were discontinued for at least five half-lives prior to the procedure. Pre-procedural cardiac enhanced computed tomography (CT) was performed to evaluate the cardiac anatomy. The surface electrocardiogram and bipolar intracardiac electrograms were continuously monitored and stored on a computer-based digital recording system (LabSystem PRO, Bard Electrophysiology, Lowell, MA, USA). The bipolar electrograms were filtered from 30 to 500 Hz. The procedure was performed under minimal or moderate sedation obtained with dexmedetomidine. A 100 IU/kg body weight of heparin was administered immediately following the venous access, and heparinized saline was additionally infused to maintain the activated clotting time at 300–350 s. A single transeptal puncture was performed using a radiofrequency needle (Baylis Medical, Inc., Montreal, QC, Canada) and 8-Fr long sheath (SLO, AF Division, SJM, Minneapolis, MN, USA).

Cryoablation group

The transeptal sheath was exchanged over a guidewire for a 15-Fr steerable sheath (Flexcath Advance, Medtronic). A spiral mapping catheter (Achieve, Medtronic) was used to advance the 28-mm second-generation CB into the PV for support and to map the PV potentials. A 23-mm CB was not used in any cases. Following the verification of complete sealing with a contrast medium injection, a freeze cycle of 180 s was applied. In order to avoid bilateral phrenic nerve injury [11], all CB applications were applied under monitoring the ipsilateral diaphragmatic compound motor action potentials during phrenic nerve pacing. If the balloon temperature reached -60°C , the freezing was terminated. The procedural endpoint was defined as an electrical PVI verified by the 20-mm circular mapping catheter (Lasso, Biosense Webster, Diamond Bar, CA, USA), and no bonus applications were performed after the isolation. Additional touch-up ablation was performed if deemed necessary.

For LCPVs, the first superior branch of the LCPV was targeted, followed by ablation of the first inferior branch, thus accepting a rather distal ablation without treatment of the antral aspect of the LCPV. To verify a complete occlusion of the targeted LCPV branch,

contrast medium was injected as described earlier. In order to analyze the technical difficulty in isolating the LCPV with a CB, the number needed to disconnect the PV (NND) was defined as the total number of freezes required to achieve an acute isolation of the LCPV.

Radiofrequency group

After a transeptal puncture, two long sheaths were introduced into both superior PVs. Following pulmonary venography during ventricular pacing, two circular mapping catheters were placed in the ipsilateral PVs, and the left- and right-sided ipsilateral PVs were circumferentially ablated guided by a 3-D mapping system (CARTO3, Biosense Webster). RF current was delivered point-by-point with a 3.5-mm externally irrigated-tip ablation catheter (Thermocool or SmartTouch, Biosense Webster) with a power of up to 35 W, target temperature of $\leq 38^{\circ}\text{C}$, and irrigation rate of 30 ml/min. The power was limited to 20 W on the posterior wall close to the esophagus. The endpoint of the procedure was an electrical PVI.

CT Scanning and measurements

Gated contrast-enhanced CT was performed with a 320-row multi-detector CT scanner (Aquilion one, Toshiba, Otawara, Japan). A bolus of 30–50 ml of iodinated contrast media was injected intravenously at an injection rate of 3.0–4.5 ml/s using an automatic injector to regulate the iodine injection speed as 22.2 mgI/kg/s. Scanning was initiated with a 10 s delay after the signal density level reached a predefined threshold of 200 Hounsfield units in the LA. Reconstructions were performed with a FC13 to generate 0.5-mm-thick slices with a reconstruction interval of 0.5 mm with a workstation (Synapse Vincent, Fujifilm, Tokyo, Japan).

The anatomy was assessed in the transverse, frontal, and sagittal planes. The ostium was defined as the point of inflection between the LA wall and PV wall. A center-line was constructed by selecting a number of points exactly in the middle of the PV in each of the three orthogonal planes. Presence of an LCPV ostium was defined as a coalescence of the inferior and superior PV of > 5 mm before the insertion into the LA. A short common PV trunk was defined as a distance from the ostium to the bifurcation of 5–15 mm, and a long common trunk as a distance of > 15 mm [7]. A strictly perpendicular plane to the ostium was used to measure the maximal and minimal diameters, and the cross-sectional area, as previously described [12,13] (Fig. 1A). The index of ovality at the PV ostial level was $2 \times (\text{maximal diameter} - \text{minimal diameter}) / (\text{maximal diameter} + \text{minimal diameter})$ [12]. Images in the axial plane were used to measure the distance of the LCPV trunk (distance from the ostium to the bifurcation) (Fig. 2A). The orientation of the LCPV trunk at the site of insertion into the LA and LCPV branches was assessed in both the transverse and frontal (coronal) planes [14]. A line was drawn in the direction of the LCPV trunk, upper LCPV branch, and lower LCPV branch in both the transverse and frontal planes. Thereafter, the angle between each PV trunk direction and the intersection line of the sagittal plane was measured in the transverse and frontal planes [14–16] (Figs. 1B–D, 2B–D).

Follow-up

No antiarrhythmic drugs were prescribed after the procedure. The patients underwent continuous, in-hospital electrocardiogram monitoring for 2–3 days following the procedure. The first outpatient clinic visit was 3 weeks after the ablation procedure. Subsequent follow-up visits consisted of a clinical interview, electrocardiograms, and/or 24-h Holter monitoring every 2–3 months at our cardiology clinic. Patients with palpitations were

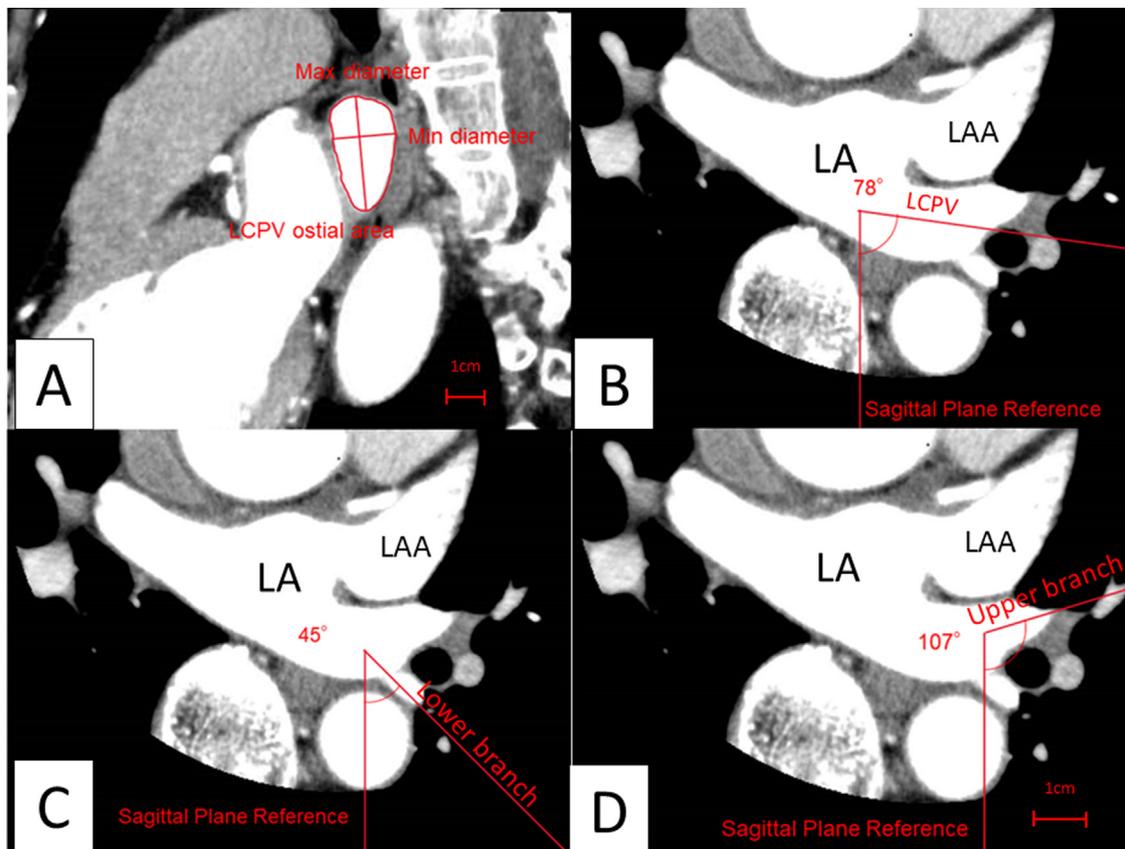


Fig. 1. The strictly perpendicular plane to the ostium was used to measure the maximal and minimal diameters, and the cross-sectional area (A). The figures display the LCPV (B), lower LCPV branch (C), and upper LCPV branch (D) orientation measurements in the transverse plane. The numbers indicate the angle between the LCPV (B), lower branch (C), and upper branch (D), and the sagittal plane reference in the transverse plane. LA, left atrium; LAA, LA appendage LCPV, left common pulmonary vein.

encouraged to use a patient-activated event recorder for one month. Recurrence was defined according to the patient's symptoms, and/or if an arrhythmia lasting longer than 30 s was documented beyond a 3-month blanking period following the latest guidelines.

Statistical analysis

Continuous data are expressed as the mean \pm standard deviation for normally distributed variables or as the median [25th, 75th percentiles] for non-normally distributed variables, and were compared using a Student's *t*-test or Mann–Whitney *U*-test, respectively. Categorical variables were compared using the chi-square test. Parameters with a significance of <0.05 in the univariate analysis were entered into a multiple logistic regression analysis to identify the factors associated with procedural difficulty. A Kaplan–Meier analysis was used to determine the percentage of patients free from recurrence. The difference in the arrhythmia-free survival was evaluated using the log-rank test. The optimal cut-off point was chosen as the combination with the highest sensitivity and specificity using receiver-operator characteristic curves. A probability value of $p < 0.05$ indicated statistical significance.

Results

Patient characteristics and procedural results

There was no significant difference in terms of the baseline patient characteristics except for the LA diameter (Table 1) or

anatomical parameters obtained from cardiac CT (Table 2) between the CB and RF groups. In the CB group, 88 of 90 (97.8%) PVs were isolated successfully with a mean of 5.6 ± 1.9 applications using exclusively 28-mm CBs. The mean number of CB applications for the LCPV, right superior PV (RSPV), and right inferior PV (RIPV) was 2.8 ± 1.3 , 1.2 ± 0.5 , and 1.6 ± 0.9 , respectively. Touch-up focal lesions were created in the remaining 2 (2.2%) PVs, including 1 LCPV and 1 RIPV. In the RF group, all PVs were successfully isolated by a point-by-point RF ablation. Cardiac tamponade occurred in 2 (3.4%) patients in the RF group, but no complications were observed in the CB group ($p = 0.308$). The total application time (15.7 ± 5.2 min vs. 29.0 ± 8.9 min, $p < 0.001$) and procedure time for achieving the PVI (43.0 ± 19.5 min vs. 68.2 ± 31.4 min, $p < 0.001$) were significantly shorter in the CB than RF group, while the total fluoroscopic time did not significantly differ between the 2 groups (23.5 ± 12.3 min vs. 28.2 ± 16.7 min, $p = 0.35$).

Factors associated with procedural difficulty in the CB procedure

Among 30 LCPVs, 1, 17, and 4 LCPVs were isolated by 1, 2, and 3 applications ($\text{NND} \leq 3$), respectively, while the remaining 8 PVs required more than 3 applications for the isolation ($\text{NND} \geq 4$). Among the parameters measured on cardiac CT, the ovality index [odds ratio (OR) = 1.136; 95% confidence interval (CI) = 1.034–1.248; $p = 0.008$], maximal LCPV diameter (OR = 1.331; 95% CI = 1.096–1.618; $p = 0.004$), and orientation difference between the LCPV and lower branch in the frontal plane (OR = 1.049; 95% CI = 1.005–1.095; $p = 0.030$) were significantly associated with an $\text{NND} \geq 4$ (Tables 3 and 4). A multivariate logistic regression analysis revealed that the ovality index (OR = 1.474; 95%

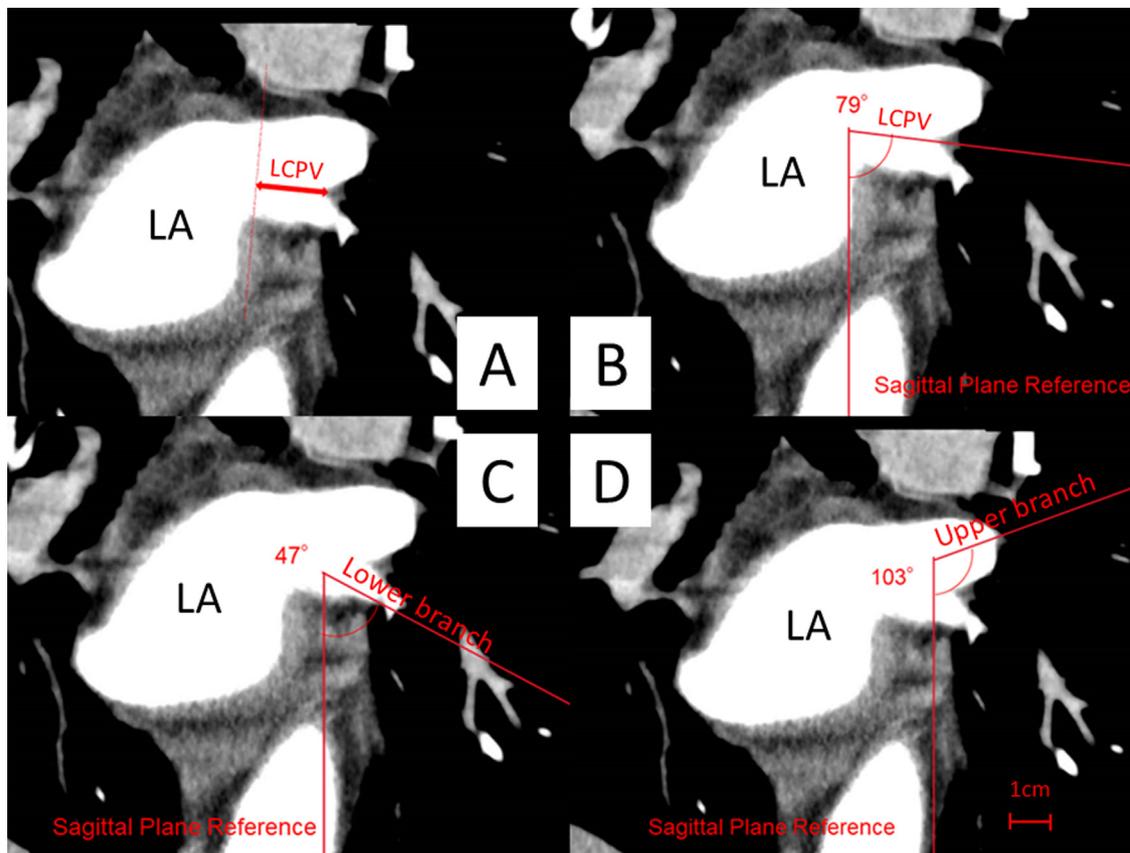


Fig. 2. Images in the axial plane were used to measure the distance of the LCPV trunk (distance from the ostium to the bifurcation) (A). The figures display the LCPV (B), lower LCPV branch (C), and upper LCPV branch (D) orientation measurements in the frontal plane. The numbers indicate the angle between the LCPV (B), lower branch (C), and upper branch (D), and the sagittal plane reference in the frontal plane. LA, left atrium; LCPV, left common pulmonary vein.

CI = 1.020–2.128; $p = 0.039$) and orientation difference between the LCPV and lower branch in the frontal plane (OR = 1.071; 95% CI = 1.008–1.137; $p = 0.026$) were independent predictors of an NND ≥ 4 (Table 4). The optimal cut-off of the ovality index and orientation difference between the LCPV and lower branch in the frontal plane were 0.59 (area under curve = 0.77) and 46.1° (area under curve = 0.75), respectively.

Clinical outcome and findings during the second procedure

During a mean of 21.4 ± 18.7 months of follow-up, the AF freedom after a single procedure was comparable between the CB and RF groups (log-rank test, $p = 0.96$). The freedom from recurrent AF at 12 months after a single procedure was 74% and 67% ($p = 0.73$) in the CB and RF groups, respectively. Among the CB group, the clinical

outcome was also similar between the patients with an NND < 3 and those with an NND ≥ 4 (log-rank test, $p = 0.63$). A second ablation procedure was performed in 6 (20.0%) and 12 (20.3%) patients at 10.0 ± 9.4 and 9.3 ± 5.0 months after index procedure in CB and RF groups ($p = 0.97$), respectively. Conduction resumption was identified in 3 (50.0%) (anterior roof, anterior bottom, and a wide anterior segment in 1 each) and 7 (58.3%) LCPVs (wide posterior segment, anterior roof, and posterior roof in 1 each, and posterior bottom and a wide anterior segment in 2 each) ($p = 0.73$), 0 (0%), and 8 (66.7%) RSPVs ($p = 0.01$), and 3 (50.0%) and 5 (41.7%) RIPVs, in the CB and RF group, respectively. Non-PV AF foci were identified in 4 (66.7%) (superior vena cava and LA posterior wall in 2 each) and 5 (41.7%) patients (LA posterior wall, crista terminalis, and right atrial anterior wall in 1 each, and superior vena cava in 2) in CB and RF groups ($p = 0.32$), respectively.

Table 1
Characteristics of the study population.

	All	CB group	RF group	<i>p</i> -value
N	89	30	59	
Age, years	64.6 \pm 9.5	66.3 \pm 9.1	63.8 \pm 9.6	0.22
Male, n (%)	59 (66.3)	18 (60.0)	41 (69.5)	0.47
Heart failure, n (%)	4 (4.5)	0 (0)	4 (6.8)	0.30
Hypertension, n (%)	49 (55.0)	14 (46.7)	35 (59.3)	0.27
Diabetes mellitus, n (%)	11 (12.3)	4 (13.3)	7 (11.9)	1.00
Left atrial diameter, mm	38 [35–42]	37.5 [34.5–40.3]	39 [35–43.5]	0.05
LV ejection fraction, %	68 [64–72]	67 [62.8–69.0]	69 [64–73]	0.21
LV diastolic diameter, mm	44 [41–48]	43 [41–46]	45 [42–48.5]	0.13

RF, radiofrequency; CB, cryoballoon; LV, left ventricular; N, number.

Table 2
Anatomical parameters of the LCPV.

	CB group	RF group	p-value
N	30	59	
LCPV ostial area, mm ²	395 [343–448]	407 [368–514]	0.16
LCPV angle (frontal),°	104.3 [97.7–115.3]	102.1 [94.8–110.1]	0.23
LCPV angle (transverse),°	81 [76.6–84.3]	79.9 [75.5–90.2]	0.88
LCPV length, mm	16.4 [13.9–18.0]	17 [14.7–18.9]	0.50
Short LCPV, n (%)	10 (33.3)	18 (30.5)	0.78
Maximal LCPV diameter, mm	28.4 [25.4–30.6]	29.0 [27.6–31.4]	0.30
Minimal LCPV diameter, mm	16.4 [14.8–17.3]	16.2 [14.6–19.6]	0.80
LCPV ovality index	0.55 [0.49–0.64]	0.53 [0.45–0.66]	0.75
Upper branch angle (frontal),°	128.1 [121.2–139.2]	133.3 [123.4–140.2]	0.39
Angle difference between LCPV and upper branch (frontal),°	22.2 [14.3–42.4]	31.7 [22.6–37.8]	0.16
Upper branch angle (transverse),°	133.2 [123.1–138.7]	132.9 [126.6–145.9]	0.59
Angle difference between LCPV and upper branch (transverse),°	52.1 [42.4–57.4]	51.4 [41.2–59.3]	0.76
Lower branch angle (frontal),°	54.7 [49.6–67.7]	61.7 [53.5–66.2]	0.53
Angle difference between LCPV and lower branch (frontal),°	45.3 [37.3–54.7]	39.7 [34.2–51.9]	0.30
Lower branch angle (transverse),°	50 [40.2–58.0]	53.7 [49.0–58.2]	0.08
Angle difference between LCPV and lower branch (transverse),°	32.4 [21.9–44.7]	27.3 [22.8–36.2]	0.54

RF, radiofrequency; CB, cryoballoon; LCPV, left common pulmonary vein.

Table 3
Anatomical parameters and number of freezing applications needed to disconnect the LCPV with a 28-mm cryoballoon.

	1–3 freezes	≥4 freezes	p-value
N	22	8	
LCPV ostial area, mm ²	399 [347.8–539]	395 [337.2–435]	0.51
LCPV angle (frontal),°	103.4 [93.8–115.3]	106.0 [99.4–115.8]	0.37
LCPV angle (transverse),°	81.8 [77–84.3]	78.0 [76.6–84.7]	0.57
LCPV length, mm	16.1 [13.8–17.3]	18.5 [15.4–20.3]	0.096
Short LCPV, n (%)	9 (40.9)	1 (12.5)	0.14
Maximal LCPV diameter, mm	27.5 [25.1–30.0]	30.1 [27.5–35.7]	0.05
Minimal LCPV diameter, mm	16.4 [15.0–17.3]	16.0 [14.3–18.7]	0.81
LCPV ovality index	0.53 [0.42–0.62]	0.62 [0.60–0.66]	0.024
Upper branch angle (frontal),°	125.4 [119.9–135.6]	136.4 [127.2–162.6]	0.07
Angle difference between LCPV and upper branch (frontal),°	22.2 [14.3–34.5]	27.3 [11.6–53.0]	0.54
Upper branch angle (transverse),°	133.9 [125–140.1]	127.6 [115.2–138.4]	0.35
Angle difference between LCPV and upper branch (transverse),°	52.1 [45.2–61.0]	48.4 [38.9–56.0]	0.51
Lower branch angle (frontal),°	55.9 [50.5–68.5]	50.9 [40.9–63.7]	0.096
Angle difference between LCPV and lower branch (frontal),°	41.7 [34.8–49.5]	50.7 [46.7–64.6]	0.039
Lower branch angle (transverse),°	49.2 [40.2–57.7]	50.3 [40.2–61.0]	0.64
Angle difference between LCPV and lower branch (transverse),°	32.9 [22.2–45.8]	25.7 [18.4–41.8]	0.40

LCPV, left common pulmonary vein.

Table 4
Anatomical parameters associated with procedural difficulty in the LCPV isolation with a 28-mm cryoballoon.

	Univariate analysis			Multivariate analysis		
	OR	95%CI	p-value	OR	95%CI	p-value
LCPV ostial area, mm ²	1.006	0.998–1.014	0.166			
LCPV angle (frontal),°	1.039	0.983–1.098	0.175			
LCPV angle (transverse),°	0.945	0.815–1.095	0.450			
LCPV length, mm	1.389	0.940–2.054	0.099			
Maximal LCPV diameter, mm	1.331	1.096–1.618	0.004			
Minimal LCPV diameter, mm	1.066	0.673–1.688	0.787			
LCPV ovality index	1.136	1.034–1.248	0.008	1.201	1.031–1.399	0.019
Upper branch angle (frontal),°	1.048	0.996–1.103	0.071			
Angle difference between LCPV and upper branch (frontal),°	1.020	0.973–1.070	0.413			
Upper branch angle (transverse),°	0.977	0.928–1.027	0.361			
Angle difference between LCPV and upper branch (transverse),°	0.984	0.940–1.030	0.488			
Lower branch angle (frontal),°	0.940	0.868–1.017	0.124			
Angle difference between LCPV and lower branch (frontal),°	1.049	1.005–1.095	0.030	1.071	1.008–1.137	0.026
Lower branch angle (transverse),°	1.007	0.940–1.079	0.841			
Angle difference between LCPV and lower branch (transverse),°	0.983	0.918–1.052	0.618			

LCPV, left common pulmonary vein; OR, odds ratio; CI, confidence interval.

Discussion

To the best of our knowledge, this is the first study to compare the procedural and clinical outcomes of PVI using second-generation CB and RF catheter in patients with an LCPV. We found that (1) the clinical outcome after the second-generation CB PVI and RF PVI was comparable in the patients with an LCPV, (2) the ovality index and difference in the orientation between the LCPV and lower branch might aid in predicting the procedural difficulty in an LCPV isolation using a 28-mm CB, and (3) the total procedure time was significantly shorter with the CB than RF ablation, but the total fluoroscopic time was similar in the patients with an LCPV between the 2 groups.

CB ablation in the patients with an LCPV

In the point-by-point RF ablation, the operator is more flexible in handling the ablation catheter and can adjust it to the PV anatomy. On the other hand, the adaptability of the CB to anatomic variations of the PVs is limited due to the fixed balloon size and geometrical shape. Since the LCPVs were isolated with a segmental superior and inferior freeze approach, the antral area might not be isolated in the CB group. Indeed, in large PVs, the PVI area during the chronic phase was significantly smaller in the CB PVI than RF PVI [17]. Therefore, the use of the CB in the setting of LCPVs is not widely accepted despite being the most commonly encountered PV anomaly in AF ablation.

Some recent studies compared the clinical outcome after a second-generation CB ablation in patients with and without an LCPV, however the results were conflicting. Ströker et al. [7] and Heeger et al. [8] showed that the clinical outcome after the CB PVI was similar in patients with and without an LCPV. On the contrary, Shigeta et al. [9] and Beiert et al. [10] demonstrated that the clinical outcome after the CB ablation was worse in patients with an LCPV than in those without. The different results presumably came from the different ablation techniques and different patient inclusion criteria, because the LCPV anatomy largely varies in individual patients. Although the comparison between the patients with and without an LCPV seems to be important, in clinical practice, the comparison between the CB and RF ablation is more important from the view point of the device selection.

The present study initially clarified that the overall clinical outcome was comparable between the CB and RF ablation in patients with an LCPV despite a significantly shorter procedure time in the CB group. Moreover, the isolation durability of the LCPV was similar between the two groups during the second procedure. These data support that, generally, a second-generation CB could be an alternative therapeutic option to RF ablation in patients with an LCPV.

Procedural difficulty of the LCPV Isolation using a CB

The isolation difficulty of the LCPV likely depends on the size, length, and angle of the branches of the LCPV [18,19]. Therefore, we explored the anatomical factors predicting the procedural difficulty in identifying better candidates for the CB ablation in the setting of an LCPV. Our study clarified that the greater ovality index predicted a higher NND in the LCPV isolation. Prior studies showed that, in first-generation CB ablation in patients with a normal PV anatomy, the extent of the ovality of the PVs correlated to adverse outcomes in terms of the efficacy [12] and isolation difficulty [13]. This is probably because an oval-shaped ostium prevents a circumferential adhesion of the CB, which results in a limited PV occlusion. However, no prior study explored the correlation between the detailed LCPV anatomy and procedural difficulty. Although the maximal LCPV diameter was not a

significant factor predicting the difficulty in the multivariate analysis, the maximal diameter tended to be larger in patients with a higher NND presumably due to the limited CB size. In addition, the orientation difference between the LCPV and lower branch in the frontal plane was significantly associated with a higher NND probably because a greater angle difference might make it difficult to obtain a stable balloon position to occlude the lower branch of the LCPV. The overall high acute success rates may reflect the fact that the operator can partially overcome the anatomical difficulty by specific handling maneuvers.

Clinical implications

The reported incidence of an LCPV in patients scheduled for a PVI was 10–30%, and is the most frequent PV variation. Our study clarified that CB ablation could be an alternative strategy to RF ablation in patients with this specific anomaly, and anatomical parameters obtained by pre-procedural imaging might aid in predicting the procedural difficulty in the LCPV isolation using a 28-mm CB. This information might be helpful for the selection of the appropriate ablation device in patients with an LCPV.

Study limitations

The study was a single center non-randomized study and the population was relatively small. The LA size tended to be slightly larger in the RF than CB group ($p = 0.05$), which might have had an impact on the study results. That was probably due to the patient selection bias, however, all LCPV cases were treated with RF catheter ablation prior to July 2014. A further prospective randomized study is warranted to validate our results.

Conclusions

The clinical outcome after the PVI in patients with an LCPV were comparable between the second-generation CB and RF ablation. The ovality index and orientation difference between the LCPV and lower branch in the frontal plane obtained on pre-procedural imaging might predict the procedural difficulty in the LCPV isolation with a 28-mm second-generation CB. This information might aid in the selection of appropriate ablation devices in the setting of an LCPV.

Financial support

None.

Disclosures

None.

Acknowledgments

We would like to thank Mr John Martin for his help in the preparation of the manuscript.

References

- [1] Haïssaguerre M, Jaïs P, Shah DC, Takahashi A, Hocini M, Quiniou G, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating from the pulmonary veins. *N Engl J Med* 1998;339:659–66.
- [2] Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm* 2017;14:e275–444.
- [3] Kojodjojo P, O'Neill MD, Lim PB, Malcolm-Lawes L, Whinnett ZI, Salukhe TV, et al. Pulmonary venous isolation by antral ablation with a large cryoballoon for treatment of paroxysmal and persistent atrial fibrillation: medium-term

- outcomes and non-randomised comparison with pulmonary venous isolation by radiofrequency ablation. *Heart* 2010;96:1379–84.
- [4] Kuck KH, Brugada J, Fürnkranz A, Metzner A, Ouyang F, Chun KR, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. *N Engl J Med* 2016;374:2235–45.
- [5] Martins RP, Hamon D, Césari O, Behaghel A, Behar N, Sellal JM, et al. Safety and efficacy of a second-generation cryoballoon in the ablation of paroxysmal atrial fibrillation. *Heart Rhythm* 2014;11:386–93.
- [6] Reddy VY, Sediya L, Petru J, Skoda J, Chovanec M, Chitovova Z, et al. Durability of pulmonary vein isolation with cryoballoon ablation: results from the Sustained PV Isolation with Arctic Front Advance (SUPIR) Study. *J Cardiovasc Electrophysiol* 2015;26:493–500.
- [7] Ströcker E, Takarada K, de Asmundis C, Abugattas JP, Mugnai G, Velagić V, et al. Second-generation cryoballoon ablation in the setting of left common pulmonary veins: procedural findings and clinical outcome. *Heart Rhythm* 2017;14:1311–8.
- [8] Heeger CH, Tscholl V, Wissner E, Fink T, Rottner L, Wohlmuth P, et al. Acute efficacy, safety, and long-term clinical outcomes using the second-generation cryoballoon for pulmonary vein isolation in patients with a left common pulmonary vein: a multicenter study. *Heart Rhythm* 2017;14:1111–8.
- [9] Shigeta T, Okishige K, Yamauchi Y, Aoyagi H, Nakamura T, Yamashita M, et al. Clinical assessment of cryoballoon ablation in cases with atrial fibrillation and a left common pulmonary vein. *J Cardiovasc Electrophysiol* 2017;28:1021–7.
- [10] Beiert T, Lodde PC, Linneborn LPT, Werner J, Prinz L, Stöckigt F, et al. Outcome in patients with left common pulmonary vein after cryoablation with second-generation cryoballoon. *Pacing Clin Electrophysiol* 2018;41:22–7.
- [11] Sacher F, Monahan KH, Thomas SP, Davidson N, Adragao P, Sanders P, et al. Phrenic nerve injury after atrial fibrillation catheter ablation: characterization and outcome in a multicenter study. *J Am Coll Cardiol* 2006;47:2498–503.
- [12] Schmidt M, Dorwarth U, Straube F, Daccarett M, Rieber J, Wankerl M, et al. Cryoballoon in AF ablation: impact of PV ovality on AF recurrence. *Int J Cardiol* 2013;167:114–20.
- [13] Ang R, Hunter RJ, Baker V, Richmond L, Dhinoja M, Sporton S, et al. Pulmonary vein measurements on pre-procedural CT/MR imaging can predict difficult pulmonary vein isolation and phrenic nerve injury during cryoballoon ablation for paroxysmal atrial fibrillation. *Int J Cardiol* 2015;195:253–8.
- [14] Gal P, Ooms JF, Ottervanger JP, Smit JJ, Adiyaman A, Ramdat Misier AR, et al. Association between pulmonary vein orientation and atrial fibrillation-free survival in patients undergoing endoscopic laser balloon ablation. *Eur Heart J Cardiovasc Imaging* 2015;16:799–806.
- [15] van der Voort PH, van den Bosch H, Post JC, Meijer A. Determination of the spatial orientation and shape of pulmonary vein ostia by contrast-enhanced magnetic resonance angiography. *Europace* 2006;8:1–6.
- [16] Sorgente A, Chierchia GB, de Asmundis C, Sarkozy A, Namdar M, Capulzini L, et al. Pulmonary vein ostium shape and orientation as possible predictors of occlusion in patients with drug-refractory paroxysmal atrial fibrillation undergoing cryoballoon ablation. *Europace* 2011;13:205–12.
- [17] Miyazaki S, Taniguchi H, Hachiya H, Nakamura H, Takagi T, Iwasawa J, et al. Quantitative analysis of the isolation area during the chronic phase after a 28-mm second-generation cryoballoon ablation demarcated by high-resolution electroanatomic mapping. *Circ Arrhythm Electrophysiol* 2016;9:e003879.
- [18] Pott A, Messemer M, Petscher K, Iturbe-Orbe M, Bothner C, Rottbauer W, et al. Clinical outcome of 2nd generation cryoballoon pulmonary vein isolation in patients over 75 years of age. *J Cardiol* 2017;69:24–9.
- [19] Yamaguchi T, Shimakawa Y, Mitsumizo S, Fukui A, Kawano Y, Otsubo T, et al. Feasibility of total intravenous anesthesia by cardiologists with the support of anesthesiologists during catheter ablation of atrial fibrillation. *J Cardiol* 2018;72:19–25.