

Efficacy of temperature-guided cryoballoon ablation without using real-time recordings – 12-Month follow-up[☆]



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ABSTRACT

Background: We sought to evaluate a temperature-guided approach of cryoballoon (CB) ablation without visualization of real-time recordings.

Methods and results: We analysed 166 patients (34.9% female, 60 ± 11 years) with paroxysmal or short-term persistent atrial fibrillation (AF). Comorbidities included diabetes mellitus (n = 28), coronary artery disease (n = 24), hypertension (n = 122), previous stroke or TIA > 3 months (n = 12). Cryoablation of the pulmonary veins (PV) was performed using first-generation (n = 78) and second-generation CB (n = 88). Two 5-minute freezes were performed for the first-generation and two 4-minute freezes for the second-generation CB with the intention to achieve a temperature drop below −40 °C. At 12-month follow-up, we observed overall freedom from AF in 92 patients (56.6%, mean time to AF recurrence 3.4 ± 2.9 months). There was a significant difference in freedom from AF between first-generation CB (45%) and second-generation CB (67%; p < 0.005). Complications were groin hematoma (4.8%) and phrenic nerve palsy (PVP) (2.4%). PVP disappeared after 12 months in all patients. Three patients developed cardiac tamponade (1.8%) that resolved without further sequelae after pericardiocentesis. Multivariate analysis revealed that only the achieved temperature in the right inferior PV (RIPV) was a predictor of long-term freedom from AF (OR 0.9; p = 0.014). Female gender was a predictor of AF recurrence (OR 6.1; p = 0.022).

Conclusion: Temperature-guided CB ablation without real-time recordings is feasible and safe without reducing the efficacy if second-generation CB is used. Deep nadir temperatures especially in the RIPV are necessary for long term-success.

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1. Introduction

Atrial fibrillation (AF) is the most important tachyarrhythmia in the developed world. It is associated with increased morbidity and mortality due to thromboembolism, heart failure and impaired cognitive functioning [1]. The prevalence and incidence of AF is increasing with age [2]. Data from randomized multicentre studies indicate that catheter ablation of AF is superior to antiarrhythmic drug therapy [3]. Current guidelines recommend catheter ablation of symptomatic paroxysmal AF in patients in whom antiarrhythmic drug therapy is ineffective and who prefer further rhythm control strategy [1]. The

cornerstone of conventional AF ablation is pulmonary vein isolation (PVI). In clinical praxis, it is the preferred technique for patients with paroxysmal and persistent AF [4–7]. Over the last years, radiofrequency (RF) current ablation in a point-by-point mode around the pulmonary vein ostia/antra was the most common method [4]. Using RF current, the cellular necrosis is achieved by tissue heating. More recently, it could be shown that cryoballoon (CB) ablation for PVI is an effective alternative to RF ablation in paroxysmal AF [8,9]. The CB ablation of the pulmonary veins (PV) is a simple, single-step approach that leads to necrosis by freezing. Before the Achieve Mapping Catheter (AC) was available for the CB, ablation was carried out “blindly” during the freezing application. A recently published study found that a temperature-guided CB ablation without using real-time recordings was effective in producing PVI and freedom from AF in 85% of patients at 12-month follow-up (FU) [10]. In our study with a larger sample size, we aimed at investigating the feasibility and efficacy of a simplified mode of CB ablation, using a solely temperature-guided approach in patients with

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paroxysmal and short-term persistent AF and further attempted to identify predictors of AF recurrence at 12-month FU.

2. Methods

2.1. Patient cohort

Patients ranging in age from 30 to 80 years, who had received the first PVI with a temperature-guided CB ablation between January 2011 and December 2014 at our centre, were consecutively included in our analysis. We included patients with symptomatic paroxysmal or short-term persistent AF. Eligibility criteria for PVI were at least one episode of AF documented by electrocardiogram (ECG) despite treatment with antiarrhythmic drugs including beta-blockers. We defined short-term persistent AF if the duration of arrhythmia was ≤ 12 months. Patients were excluded if they had previously undergone ablation in the left atrium (LA), if their LA was >55 mm in diameter, or if there was evidence of LA thrombus. Furthermore, patients were excluded if they had unstable angina, myocardial infarction, percutaneous transluminal coronary angioplasty or cardiac surgery within the previous three months, heart failure grade IV (New York Heart Association criteria), stroke or transient ischemic attack within the previous 6 months, pregnancy or life expectancy < 1 year. All patients provided written informed consent prior to the intervention.

2.2. Study procedure

Baseline evaluation of patients comprised clinical history, review of medication, physical examination, blood chemistry, and 12-lead ECG. In order to exclude LA thrombi, transesophageal echocardiogram was performed in all patients at the day of intervention. Procedures were carried out under moderate sedation with midazolam and fentanyl. Single transseptal puncture was performed using a SL1 introducer sheath (ST Jude Medical, Minnetonka MN, USA). Immediately after having positioned the transseptal sheath across the interatrial septum, therapeutic anticoagulation was initiated with boluses of heparin. During the procedure, activated clotting time was maintained 300–350 seconds (s). Thereafter, the SL1 sheath was exchanged for a 12 french (F) FlexCath sheath (CryoCath, Medtronic Inc., Minneapolis, MN, USA). After PV angiography, CB was positioned in the left atrium. Cryoablation of the PVs was then performed using the first-generation CB (Arctic Front, Medtronic Inc.) for the first 78 procedures and the second-generation CB (Arctic Front Advance, Medtronic Inc.) for the last 88 procedures. The selection of CB size (23 mm vs. 28 mm) was left to the discretion of the operator. After the CB was applied to the PV ostium, contrast dye was injected through the central lumen of the CB to ensure an adequate “seal” and an occluded PV ostium. Optimal vessel occlusion was achieved when contrast dye injection showed complete contrast retention without backflow to the left atrium (vessel occlusion was evaluated in a semi quantitative manner ranging from grade 0 (very poor) and 4 (perfect)). With the intention to achieve at least a temperature drop below -40 °C, at least two 5-minute freezes were performed for the first-generation and two 4-minute freezes were performed for the second-generation CB according to the manufacturer's recommendation. Additional applications could be used if deemed necessary. During CB ablation of the right PVs phrenic nerve injury was monitored using phrenic nerve pacing or breathing manoeuvres. If signs of phrenic nerve injury occurred, CB ablation was stopped immediately.

All patients received oral anticoagulation therapy during the first three months after the procedure, and thereafter according to the CHA₂DS₂-VASc-Score. After three months, anticoagulation was only discontinued in patients with a CHA₂DS₂-VASc-Score of ≤ 1 for men and ≤ 2 for women. Follow-up (FU) assessments were performed at three, six and 12 months during visits in our outpatient clinic. Antiarrhythmic drug therapy was stopped in all patients at least at 3-months FU. Additional visits were performed if patients were symptomatic or AF

has been documented (12-lead-ECG or Holter ECG). Clinical and biochemical evaluation, as well as Holter ECG were carried out at baseline and at each FU visit. Each documented episode of ≥ 30 s after the three months blanking period was considered a failure. Furthermore procedural data, total radiation exposure, and occurrence of adverse events including phrenic nerve palsy (PNP), pericardial effusion, stroke, and vascular complications were reviewed.

2.3. Statistical analysis

Continuous variables are shown as mean \pm standard deviation (SD). Categorical data are summarized as frequencies and percentages. Differences in baseline characteristics among patients were analysed with an unpaired Student's *t*-test for continuous variables and with χ^2 or Fisher's exact test for proportions, respectively. Event curves were determined according to the Kaplan-Meier method, with comparisons of cumulative event rates by the log-rank test. A multivariate logistic regression model was estimated to adjust for potential confounding factors for arrhythmic events, such as age, gender, aetiology, New York Heart Association (NYHA) functional class, left atrial size, left ventricular ejection fraction (LVEF), or beta-blocker treatment. In the multivariate model, continuous covariates were categorized according to age (in 10-year steps) and LVEF (in 5% steps). The multivariate analysis was also repeated without categorizing covariates. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated as an estimate of recurrent arrhythmic events.

All tests of statistical significance were 2-tailed, and a *p* value < 0.05 was considered statistically significant. The analyses were computed with SPSS software version 19 (SPSS Inc., Chicago, IL, USA) statistical software.

3. Results

3.1. Demographics

We performed simplified anatomical- and temperature-guided CB ablation without real-time recordings in 166 patients (34.9% female, mean age 60 ± 11 years) with paroxysmal (62%) or short-term persistent AF (38%). Mean fluoroscopy time was 12.7 ± 5.6 min. Patients had the following co-morbidities: 24 patients with coronary artery disease (14.5%), 12 patients with previous stroke or TIA > 3 months (7.2%), 28 patients with diabetes mellitus (16.9%), 11 patients with chronic renal insufficiency (6.6%), and 122 patients with hypertension (73.5%). Mean left ventricular ejection fraction (LVEF) was $63.0 \pm 11.4\%$, mean left atrial diameter (LAD) was 45.1 ± 8.3 millimetre (mm), mean diastolic interventricular septum thickness (IVSd) was 11.7 ± 2.5 mm. Mild to moderate mitral valve regurgitation (MR) was observed in 68.1% of patients, and 47.0% of patients had mild to moderate tricuspid valve regurgitation (TR). The mean CHA₂DS₂-VASc-Score was 2.1 ± 1.5 . Baseline parameters of patients are shown in [Table 1](#).

3.2. Clinical outcomes

During the 12 months of FU, we observed freedom from AF in 92 patients (56.6%). There was a significant difference in freedom from AF between first-generation CB (45%; 43 out of 78 patients) and second-generation CB (67%; 29 out of 88 patients; *p* < 0.005). The mean time to AF recurrence was 3.4 ± 2.9 months. The results are shown in [Fig. 1](#). The most common complications were groin-site complications that occurred in 4.8% of the cases (8 patients with hematoma) and phrenic nerve palsy (PNP) that occurred in 2.4% of the cases (4 patients). PNP disappeared after 12 months in all patients. Three patients developed cardiac tamponade (1.8%) that resolved without further sequelae after uncomplicated pericardiocentesis. No stroke, arterioesophageal fistula, pulmonary vein stenosis or death occurred.

Four patients experienced cavotricuspid isthmus (CTI)-dependent atrial flutter during the blanking period. Ablation of the CTI was

Table 1
Baseline clinical characteristics of patients.

Parameter; mean ± SD or n (%)	All patients (n = 166)	Freedom from AF (n = 94)	Recurrence of AF (n = 72)	p value
Female gender	58 (34.9)	27 (28.7)	31 (43.1)	0.055
Age (years)	60 ± 11	60 ± 11	60 ± 11	0.650
BMI (kg/m ²)	28.9 ± 4.78	28.3 ± 4.77	29.6 ± 4.74	0.081
Heart rate	77.0 ± 24	73.9 ± 20	81.0 ± 29	0.060
Paroxysmal AF	102 (61.5)	61 (64.9)	41 (56.9)	0.353
Persistent AF	63 (38.0)	33 (35.1)	30 (41.7)	0.353
CAD	24 (14.5)	12 (12.8)	12 (16.7)	0.479
Stroke/TIA	12 (7.2)	5 (5.3)	7 (9.7)	0.278
Diabetes mellitus	28 (16.9)	19 (20.2)	9 (12.5)	0.189
Chronic renal insufficiency	11 (6.6)	7 (7.4)	4 (5.6)	0.618
Hypertension	122 (73.5)	67 (71.3)	55 (76.4)	0.460
Obstructive sleep apnoea	9 (5.4)	3 (3.1)	6 (8.3)	0.147
CHA ₂ DS ₂ -VASC-Score	2.1 ± 1.5	2.0 ± 1.6	2.2 ± 1.4	0.460
NYHA classification				
Class ≤ I	98 (59)	63 (67)	35 (49)	0.016
Class II	48 (29)	21 (22)	29 (40)	0.004
Class III	20 (12)	10 (11)	8 (11)	0.922
Fluoroscopy time	12.7 ± 5.6	12.1 ± 5.2	13.4 ± 6.1	0.167
Contrast dye	100.3 ± 40.0	96.5 ± 35.3	105.3 ± 44.9	0.164
Echocardiographic parameters				
LAD (millimeter)	45.1 ± 8.3	44.4 ± 8.1	45.8 ± 8.5	0.446
LVEF (%)	63.0 ± 11.4	65.2 ± 11.2	60.4 ± 11.1	0.030
IVSd (millimeter)	11.7 ± 2.5	11.6 ± 2.6	11.8 ± 2.2	0.666
Medication				
Betablocker	146 (88.0)	81 (86.2)	65 (90.3)	0.420
ACE-I/ARB	98 (59.0)	58 (62.0)	51 (57.0)	0.632
Adosterone antagonists	2 (1.2)	1 (1.1)	1 (1.4)	0.849
Diuretics	63 (38.0)	42 (44.7)	22 (30.6)	0.086
Statins	47 (28.3)	28 (29.8)	19 (26.4)	0.630
Calcium-channel blockers	7 (4.2)	4 (4.3)	3 (4.2)	0.978
Antiarrhythmic drugs				
Flecainide	65 (39.2)	36 (38.3)	29 (40.3)	0.796
Amiodarone	49 (29.5)	27 (28.3)	23 (31.9)	0.654
Dronedaron	8 (4.8)	6 (6.9)	2 (2.8)	0.282
Flecainide "pill in the pocket"	2 (1.2)	2 (2.1)	0 (0)	0.213
Anticoagulation drugs				
Phenprocumon	80 (48.2)	44 (46.8)	36 (50.0)	0.683
Rivaroxaban	45 (27.1)	24 (25.5)	21 (29.2)	0.602
Dabigatran	28 (16.9)	19 (20.2)	9 (12.5)	0.188
Apixaban	8 (4.8)	7 (7.5)	1 (1.4)	0.071

BMI: Body mass index; AF: atrial fibrillation; CAD: coronary artery disease; TIA: transient ischemic attack; NYHA: New York Heart Association Functional Classification; LAD: left atrial diameter, LVEF: left ventricular ejection fraction; IVSd: diastolic interventricular septum thickness; ACE-I: angiotensin-converting enzyme-inhibitor; ARB: angiotensin receptor blocker; CHA₂DS₂-VASC score: clinical estimation of the risk of stroke in patients with atrial fibrillation ranging from 0 to 9. Higher scores indicate a greater risk. p value for heterogeneity between AF recurrence and no AF recurrence group. Differences in baseline characteristics among patients were analysed with an unpaired Student's *t*-test for continuous variables and with χ^2 or Fisher's exact test for proportions.

performed with nonirrigated RF energy catheter in all four patients within the blanking period. In our analysis, these cases were not classified as a failure of cryoballoon ablation.

3.3. Predictors of long-term freedom of AF

Univariate analysis showed that those patients with better NYHA functional class, better LVEF (65.2 ± 11.2 vs. 60.4 ± 11.1) and patients in whom a deeper mean temperature in the PVs was achieved had significant lower recurrence rates of AF. We found no differences in medical treatment between patients with and without recurrence of AF (Tables 1 and 2). However, multivariate analysis found that only the achieved temperature in the right inferior PV (RIPV), but not in the left superior PV (LSPV), left inferior PV (LIPV), and right superior PV (RSPV) was a predictor of long-term freedom from AF (OR 0.9, 95% CI 0.8–1.0; *p* = 0.014). Co-morbidities like NYHA functional class, coronary artery disease (CAD), diabetes mellitus, or hypertension as well as echocardiographic parameters like LAD and IVSd were not associated with AF recurrence following CB ablation. Female gender was a predictor of AF recurrence after CB ablation of the PVs (OR 6.1, 95% CI 1.3–29.5; *p* = 0.022). The results are shown in Table 3.

4. Discussion

To our knowledge, this is the largest real-life study of a simplified combined anatomical- and temperature-guided CB ablation of the PV without real-time recordings. The main findings of our study are the following: A temperature-guided CB ablation of the PVs without the use of real-time recordings in patients with paroxysmal or short-term persistent AF is feasible, safe, and effective during 12 months of FU. The overall success rate in our patient group defined as freedom from AF at 12-month FU after the procedure was lower in comparison to recent randomized trials. However, the success rate between first- and second-generation CB differed substantially. The long-term success rate by using the second-generation CB was comparable with recent randomized CB trials [9]. The achieved temperature in the RIPV was a predictor for long-term freedom from AF. Female gender was associated with an increased risk for AF recurrence.

At the beginning of the CB ablation for PVI in AF, no inner-lumen mapping-catheter was available. Ablation was done without real-time monitoring of PV potentials during the procedure and PV potentials could only be mapped after CB ablation. During that time, the CB was technically modified with implementation of a higher number of injection ports that are positioned more distally and further,

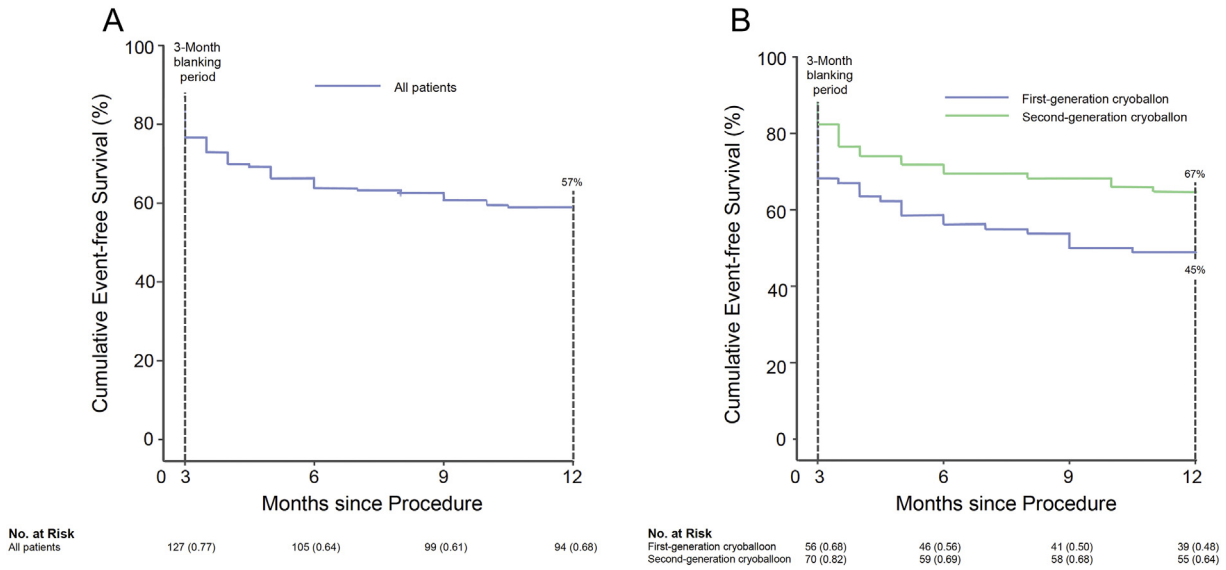


Fig. 1. Kaplan-Meier estimates of time to first AF recurrence in the study. The first 3 months after ablation was the so-called “blinking period”. Events during this time were not counted in the determination of AF recurrence, except in those patients who did not maintain sustained sinus rhythm after medical treatment or electrical cardioversion. Panel A shows the overall success rate of freedom from AF. Freedom from AF was observed in 56.6% of the patients. The mean time to AF recurrence was 3.4 ± 2.9 months. Panel B shows the subgroup test of success rate among first- and second-generation CB. There was a significant difference in freedom from AF between first-generation CB (45%; 43 out of 78 patients) and second-generation CB (67%; 29 out of 88 patients; $p < 0.005$).

the inner-lumen AC mapping catheter was introduced into clinical praxis.

The use of the second-generation CB in line with the inner-lumen AC mapping catheter led to a significant improvement of acute PVI [11]. Currently, the single catheter CB ablation in combination with the AC is the standard approach in CB ablation. The AC is a CB guidewire that allows simultaneous mapping of PV potentials during the freezing.

Ablation and mapping of the PVs can be done with only one transeptal puncture and without the need of catheter changes during the procedure. However, the verification of ostial PVIs using the AC might not always be sufficient to confirm ostial PVI in an accurate manner [12]. Recently Miyazaki et al. reported that the accuracy in verification of ostial PVIs with the AC ranged between 75% and 89%, depending on the location of the PV [12]. Meissner et al. compared the number of PV potentials recorded either by 32-pole high-density mash mapper (HDMM) or by 8-pole AC. Despite a significant difference in the identification of PV potentials before and after the CB ablation, the outcome between the standard group (AC mapping only) and the study group (additional HDMM mapping) by means of freedom from AF was similar at 3 (82% vs 83%) and at 6 months (79 vs 76%) [13]. This refers to the question whether a simplified method of a solely combined

anatomical and temperature-guided PVI without measurement of real-time recordings might be feasible and effective during long-term FU.

The use of a J-tip guidewire instead of the AC might have some advantages. The J-tip guidewire is more flexible in comparison to the AC. Thus, it seems to be far easier to negotiate smaller PV branches that might lead to a better CB positioning in the PV ostium. Furthermore, the use of the AC in smaller PV branches could be more dangerous, since few cases of fracture of the AC in a PV branch during PVI and intramural PV hematoma following PVI have been reported [14,15]. It is further noteworthy that CB ablation by using a J-tip guidewire is much cheaper than CB ablation with AC given the need of reducing health care costs. This point should not be underestimated.

Table 2
Achieved temperatures in the pulmonary veins.

Mean temperature (freeze application)	All patients (n = 166)	Freedom from AF (n = 94)	Recurrence of AF (n = 72)	p value
LSPV (I)	-43.0 ± 7.9	-44.1 ± 7.8	-41.6 ± 7.7	0.046
LSPV (II)	-44.9 ± 7.3	-46.1 ± 7.0	-43.4 ± 7.5	0.022
LIPV (I)	-40.5 ± 7.1	-41.7 ± 7.5	-39.0 ± 6.3	0.016
LIPV (II)	-40.8 ± 7.1	-41.6 ± 7.8	-39.4 ± 5.7	0.059
RSPV (I)	-44.7 ± 7.2	-45.5 ± 7.5	-43.7 ± 6.6	0.121
RSPV (II)	-45.6 ± 6.7	-46.6 ± 7.2	-44.0 ± 5.4	0.033
RIPV (I)	-41.0 ± 7.9	-41.8 ± 8.1	-39.8 ± 7.4	0.138
RIPV (II)	-42.2 ± 8.0	-43.4 ± 8.6	-40.3 ± 6.5	0.041

LSPV: left superior pulmonary vein; LIPV: left inferior pulmonary vein, RSPV: right superior pulmonary vein; RIPV: right inferior pulmonary vein. p value for heterogeneity between AF recurrence and no AF recurrence group. Differences in baseline characteristics among patients were analysed with an unpaired Student's t-test for continuous variables.

Table 3
Multivariate logistic regression model for freedom from atrial fibrillation.

Variable	OR (CI 95)	p value
NYHA classification	0.8 (0.3–2.5)	0.722
Female gender	6.1 (1.3–29.5)	0.022
LAD	1.0 (0.9–1.1)	0.373
IVSD	1.0 (0.7–1.4)	0.987
CAD	3.6 (0.5–28.4)	0.208
Diabetes mellitus	0.2 (0.02–1.4)	0.089
Hypertension	2.3 (0.2–23.0)	0.473
ACE inhibitor	0.7 (0.1–5.2)	0.742
Fluoroscopy time	1.1 (1.0–1.2)	0.216
<i>Temperature</i>		
LSPV	1.1 (1.0–1.2)	0.229
LIPV	1.1 (1.0–1.2)	0.086
RSPV	1.1 (1.0–1.2)	0.121
RIPV	0.9 (0.8–1.0)	0.014

NYHA: New York Heart Association Functional Classification; LAD: left atrial diameter; LVEF: left ventricular ejection fraction; IVSD: diastolic interventricular septum thickness; CAD: coronary artery disease; ACE-I: angiotensin-converting enzyme-inhibitor; ARB: angiotensin receptor blocker; LSPV: left superior pulmonary vein; LIPV: left inferior pulmonary vein, RSPV: right superior pulmonary vein; RIPV: right inferior pulmonary vein. Odds ratios (OR) with 95% confidence intervals (CI) were calculated as an estimate of AF freedom at 12 months. The achieved temperature in the RIPV was a predictor for long-term freedom from AF. A female gender was associated with an increased risk for AF recurrence.

Recently, Iacopino et al. published the results of a temperature-guided strategy to CB ablation [10]. The authors compared the long-term efficacy of PVI in patients with paroxysmal AF ($n = 52$) who received second-generation CB ablation with a temperature-guided approach in comparison with a propensity score matched group of patients ($n = 52$), in whom the CB ablation was performed with the inner-lumen AC. With the goal to achieve a temperature drop below -40°C within 60 s, the authors found acute PVI in 99% of the cases. Despite of the fact that we did not check the PVs with a mapping catheter for PV potentials, the need of a temperature drop below -40° for successful ablation is in agreement with the long-term results in our study population. Patients without recurrent AF had a mean temperature drop below -40°C , whereas patients with recurrent AF had not. In the study of Iacopino et al. the long-term success rate after a median of 12 months was 85% in the wire group and 88% in the AC group [10]. This success rate was higher in comparison to our overall results with first- and second-generation CB together (AF freedom for all patients was 57% after 12 months), but also much higher as in recent multicentre randomized trials with larger patient samples, in which 65.4% of patients were free of AF at 12 months (FIRE AND ICE), respectively 67% of patients (The Cryo versus RF Trial) [9,16]. The results of these trials are, however, comparable to our results in those patients, who received ablation with second-generation CB (AF freedom in patients treated with the second-generation CB was 67%). In contrast to our study, Iacopino et al. checked PVs for remaining PV potentials, even in the temperature-guided group. Patients with remaining PV potentials received further cryoapplications [10]. Because of this, the results of this study are not really only temperature-guided and the long-term results of freedom from AF are therefore not completely comparable with our results. According to the baseline characteristics, our patients had also higher rates of hypertension, diabetes mellitus, CAD, and chronic kidney disease in comparison to the patients in the studies of Kuck et al. and Iacopino et al. [9,10]. In addition, we included patients with paroxysmal AF and also with short-term persistent AF in our analysis that might have led to the lower long-term success rate, as shown formerly [17,18]. In recent trials, success rate at 12-month FU in persistent AF patients was 50% by using first-generation CB [19] and 69% by using second-generation CB [20]. Only few data exist about CB-based PVI in a mixed cohort of patients with paroxysmal and persistent AF. Recently, three-year clinical outcome data after second-generation CB-based PVI have been published. The study included patients with paroxysmal (70%) and persistent AF (30%). After a median FU of 38 months 60% of patients remained in stable sinus rhythm. However, in comparison to our results with 38% of patients with persistent AF, the success rate in this trial was higher at 12 months (nearly 80%). But it was also much higher than the success rate at 12 months FU in the multicentre randomized "FIRE AND ICE" trial [9,21].

The temperature drop during CB ablation depends on anatomical conditions, the operator dexterity, and experience. Recent studies found that the achieved nadir temperature during CB ablation is of major importance for the success rate of CB ablation in patients with AF [11,22]. Our results support these findings. Univariate analyses demonstrated that the achieved temperatures in the LSPV, LIPV, RSPV, and RIPV were predictors of freedom from AF following CB ablation. However, multivariate analysis found that only the achieved temperature in the RIPV was significant. The fact that especially the achieved temperature in the RIPV predicts freedom from AF is a new and interesting finding. A perfect closure, especially of the RIPV, is for anatomic reasons sometimes difficult to achieve. According to our results, it seems necessary to make intensive efforts to reach deep nadir temperatures, especially in the RIPV.

Since PVI is expensive and associated with small but definite risk of serious complications, the prediction of the outcome of patients before PVI is of particular interest. In patients with AF, cardiovascular risk factors such as diabetes mellitus, CAD, hypertension, or obesity often occur simultaneously. Consequently, we additionally investigated the impact of these co-existing risk factors on the success-rate of CB

ablation in paroxysmal and short-term persistent AF. In the multivariate analysis, only female gender predicted AF recurrence, whereas the above-mentioned confounding factors as well as left atrial diameter or interventricular septum thickness did not. This is in contrast to the results of the study of Winkle et al., who found that patients with pre-existing diabetes, hypertension, CAD, LA diameter or persistent AF were strong predictors of AF recurrence following AF ablation [23]. However, current guidelines do not recommend exclusion of patients with the aforementioned risk factors [1].

Our study is limited by the fact that it is a small non-randomized trial with a heterogeneous patient cohort (persistent and paroxysmal AF). But it shows real-life data with the largest patient sample ever studied, with a simplified combined anatomical- and temperature-guided CB ablation of the PVs with 12 months of FU. Our results clearly show that PVI with CB without real-time monitoring of PVPs is feasible and effective with comparable results of AF freedom in long term FU, if the second-generation CB is used. This approach of CB-ablation reduces procedural costs and simplifies the procedure, without reducing the efficacy. Further randomized trials should evaluate whether there is a nadir temperature that should be necessarily reached to achieve a definite acute PVI. Intensive efforts should be undertaken to reach deep nadir temperatures and the best possible occlusion, especially in the RIPV.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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