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Clinical outcome and left atrial function after left atrial roof ablation using the cryoballoon technique in patients with symptomatic persistent atrial fibrillation

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ABSTRACT

Introduction: There are no data concerning clinical outcome and left atrial (LA) function after LA roof ablation using a second-generation cryoballoon (CB) for treatment of persistent atrial fibrillation (AF). Here, we report the first follow-up results after pulmonary vein isolation (PVI) plus LA roof ablation with the CB technique in patients with symptomatic persistent AF.

Methods and results: We enrolled 107 consecutive patients who underwent CB ablation at our institution with the aim of PVI and bidirectional conduction block across the LA roof. Clinical success was defined as freedom from >30-s recurrence of AF, atrial flutter, or atrial tachycardia after a 3-month blanking period. Follow-up data were collected during outpatient clinic visits. LA volume, LA emptying fraction, and LA expansion index (parameters of LA function) were evaluated by echocardiography before and 3 months after ablation.

PVI was achieved in all patients, and bidirectional conduction block was verified in 91.6%. Median follow-up duration was 31 (interquartile range 11/44) months. PVI plus LA roof ablation was sufficient to restore and maintain sinus rhythm in 72.9% ($n = 78$) of patients. The overall complication rate was 1.8%. LA volumes decreased significantly after ablation ($P < 0.05$), whereas total LA emptying fraction ($P = 0.25$) and LA expansion index ($P = 0.32$) were preserved within the 3-month follow-up.

Conclusions: LA roof ablation combined with PVI using the CB technique is a safe and effective adjuvant treatment with a promising midterm outcome and preserved LA function 3 months after ablation.

1. Introduction

Cryoballoon (CB) pulmonary vein isolation (PVI) is a well-recognized treatment for paroxysmal atrial fibrillation (AF) [1]. The second-generation CB (CB-Adv), introduced in 2012, has shown good mid- and long-term clinical outcomes [2,3]. CB-Adv PVI is increasingly used for persistent AF, but PVI alone is sometimes insufficient, possibly because atrial fibrosis extent and atrial remodeling progression increase with every AF episode [4,5]. Several additional ablation strategies may enhance clinical outcome [6,7], but there are limited data using CB beyond ostial and antral PVI. Combining PVI with left atrial (LA) roof ablation using a CB is reportedly feasible and safe in persistent AF patients [8], but conclusive follow-up data are unavailable. Furthermore, the effect of roof ablation on LA function has not been sufficiently evaluated. Here, we assessed the clinical outcome of PVI plus LA roof ablation using the CB-Adv, and its impact on LA function.

2. Methods

2.1. Study population

Consecutive patients with symptomatic persistent AF who underwent CB-Adv PVI plus LA roof ablation from June 2013 onwards at the Kerckhoff Heart Center were retrospectively analyzed. Mainly patients with LA enlargement (according to guidelines [9]) or persistent AF after PV isolation were selected for an additional LA roof ablation by the investigator performing the procedure. Patient medical records, including ECGs and Holter-ECG recordings of AF episodes, were thoroughly reviewed. Patients were also questioned about arrhythmia-related symptom intensity and duration. Exclusion criteria were severe valvular disease, LA thrombus, reversible causes of AF, myocardial infarction or cardiac surgery in the previous 3 months, known bleeding diathesis or intolerance to heparin or oral anticoagulation, previous AF ablation, pregnancy, severe comorbidity, or New York Heart Association class IV heart failure. All patients provided written informed consent prior to the procedure.

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2.2. Preprocedural echocardiography

Preprocedural transthoracic and transesophageal echocardiography was performed by trained operators to assess cardiac dimensions and function and exclude the presence of LA appendage thrombi (Philips iE33 system, Philips Medical Systems, Hamburg, Germany). The images were stored on digital media for subsequent analysis using TomTec Auto LA™ software (TomTec Imaging Systems, Unterschleissheim, Germany). All measurements were acquired over 3 consecutive beats during sinus rhythm (SR). LA volumes (LAVs) were obtained by two-dimensional echocardiography using the biplane area-length method as described by Lang et al [9]. LA areas (A_1, A_2) and superoinferior longitudinal diameters were measured from apical 4- and 2-chamber views. LAVs were calculated as $[(8/3\pi) A_1A_2]/L$, where L is the shorter superoinferior LA diameter. Maximum (LV end-systole, just before mitral valve opening), minimum (LV end-diastole at the start of QRS), and pre-systolic LAVs (at peak of P wave of simultaneously recorded electrocardiogram) were indexed to body surface area (calculated by the Dubois formula, using body height and weight).

Total LA emptying fraction (LAEF), LA active emptying fraction (LAAEF), LA passive emptying fraction (LAPEF), and LA expansion index (LAEI) were calculated from phasic volumes: $LAEF = 100\% \times (LAV_{max} - LAV_{min})/LAV_{max}$, $LAAEF = 100\% \times (LAV_{pre\text{-}systolic} - LAV_{min})/LAV_{pre\text{-}systolic}$, $LAPEF = 100\% \times (LAV_{max} - LAV_{pre\text{-}systolic})/LAV_{max}$, and $LAEI = 100\% \times (LAV_{max} - LAV_{min})/LAV_{min}$.

Newer methods of evaluating LA function (e.g., color-coded tissue-Doppler-based strain and strain rate and two-dimensional speckle-tracking-based strain and strain rate) were unavailable for most of the patients during study enrollment.

2.3. Ablation procedure

Ablation was performed on patients under conscious sedation or general anesthesia with a 28-mm CB-Adv (Arctic Front Advance™, Medtronic, Minneapolis, MN, USA). In a subset of 10 patients, esophageal temperature was continuously monitored throughout the procedure with a temperature probe (SensiTherm, Abbott, Chicago, IL, USA). After single transseptal access (SL-1 sheath, Abbott, Chicago, IL, USA) by the modified Brockenbrough technique (BRK-1, Abbott), an exchange wire was placed in the left superior pulmonary vein (PV), and the SL-1 sheath was replaced with a steerable 15 Fr sheath (FlexCath Advance™, Medtronic). LA and PV anatomies were visualized by PV angiography. The LA and PV borders including the PV ostia and transseptal puncture site (determined by PV angiography) were marked on the monitor screen for easier manoeuvring and positioning of the CB during the ablation procedure. Pulmonary vein (PV) signals were mapped with an inner lumen spiral mapping catheter (Achieve catheter™, 20-mm diameter, Medtronic) before, during, and after each cryoenergy application according to standard procedures. Diagnostic mapping was conducted with a decapolar catheter (IBI, Abbott, Chicago, IL, USA). Guided by the Achieve™ catheter, the CB-Adv was advanced through the sheath into the LA, inflated proximal to the PV ostium, and then gently pushed to seal off the PV. Vessel occlusion and atrial backflow were evaluated by selective injection of contrast medium. After the best possible occlusion was achieved, a 180-s freeze–thaw cycle was performed. If online isolation occurred later than 90 s or if online signals were unavailable, a 240-s freeze–thaw cycle was performed. During septal PV ablation, the decapolar catheter was positioned in the superior vena cava for ipsilateral phrenic nerve pacing. Phrenic nerve function was monitored using diaphragmatic compound motor action potentials (CMAPs) [10]. Refrigerant delivery was immediately terminated if CMAP decreased by 40%, indicating weakening or loss of diaphragmatic contraction.

An additional LA roof ablation was performed in all patients as described before [8]. Briefly, sequential overlapping 180-s freezes were applied (starting near the position used for left superior PV isolation) along the LA roof by slight clockwise rotation combined with slight sheath retraction and incremental advancement of the CB-Adv until the position used for right superior PV isolation was reached [8]. The Achieve catheter was anchored in the left superior PV for all CB-Adv positions at the LA roof.

In AF patients without intraprocedural conversion to SR, electrical cardioversion was performed, and then PVI and conduction block at the LA roof were verified. The procedural endpoint was complete PVI and conduction block across the LA roof and ascending activation across the posterior LA wall. Therefore, the Achieve catheter was positioned at the caudal (Fig. 1A + B) and cranial posterior LA wall (Fig. 1D + E) guided by the steerable sheath. Subsequently, baseline pacing during SR at the right atrial upper septum with a cycle length of 500 ms was performed. Activation times at the caudal (Fig. 1C) and cranial position (Fig. 1F) of the posterior LA wall next to the LA roof were measured. A caudocranial ascending activation at the posterior LA wall and a >120-ms conduction delay next to the ablation area verified conduction block of the LA roof.

Patients with documented typical right atrial flutter prior to the procedure or periprocedural typical atrial flutter received an additional cavotricuspid isthmus radiofrequency (RF) ablation (3.5-mm irrigated-tip catheter; Thermocool, Biosense Webster, Diamond Bar, CA, USA). No RF ablations targeting extrapulmonary foci were performed, and no additional linear lesions were created.

2.4. Postprocedural management

Pericardial effusion was excluded by echocardiography immediately after ablation. After removal of the large venous sheaths, the access site was closed by manual compression or subcutaneous temporary purse-string suture [11]. Patients were monitored telemetrically for ≥24 h. In patients with persistent postprocedure phrenic nerve palsy (PNP), phrenic nerve function was assessed via chest fluoroscopy of diaphragmatic movement prior to hospital discharge. Periprocedural complications were defined as described previously [12].

2.5. Follow-up

Clinical success was defined as freedom from >30-s AFLAT (AF, atrial flutter, or atrial tachycardia) recurrence after the 3-month blanking period in the absence of antiarrhythmic drugs (AADs). Our strict follow-up protocol is consistent with the latest recommendations [12]. Patients were monitored via resting ECG, 7-day Holter-ECG (analyzed by a core lab) and echocardiography during follow-up visits at 3- month or 6-month intervals in the first year. Late follow-up (>1 year post-intervention) was performed once a year. Additional adverse events and complications were assessed by structured telephone interviews. Echocardiographic parameters were evaluated 3 months postablation in all patients, and in case of pathological findings or clinical symptoms during further follow-up. For arrhythmias during the blanking period, AADs were prescribed until the 3-month follow-up and then discontinued. Patients with highly symptomatic drug-refractory AFLAT recurrence after the blanking period were evaluated for repeat ablation with a RF catheter, including voltage mapping guided by an electroanatomic mapping system.

2.6. Statistical analysis

Continuous data are presented as means or medians with standard deviations and interquartile ranges (IQRs), and categorical variables are given as numbers and percentages. The effects of discrete variables were studied using Kaplan-Meier survival analysis with the log-rank test. Differences between continuous variables were assessed using a Mann-Whitney U test or Kruskal-Wallis test. Two-tailed P-values <0.05 were considered statistically significant. Statistical analyses were performed using SPSS software (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Baseline and procedural characteristics

In all 107 patients (Table 1 with baseline characteristics), complete circumferential PVI and additional roof ablations were achieved with the CB-Adv without RF-based touch-up lesions (Table 2). The nadir luminal esophageal temperature during LA roof ablation (in the subset of 10 patients in whom esophageal temperature was measured) was 23 °C. We isolated 430 PVs with a median of 8 (IQR 6/9) freezes per patient. A bonus freeze was applied in the first 67 patients. Procedure and fluoroscopy times decreased every year: from 132 (120/149) min in 2013 to 91 (80/112) min in 2017 ($P < 0.001$) and from 25 (22/29) min in 2013 to 14 (12/22) min ($P = 0.003$) in 2017, respectively. Conduction block across the LA roof was confirmed in 98 (91.6%) patients. In 5 of the remaining 9 patients, LA roof block could not be determined owing to persistent postprocedure AF without conversion to SR after cardioversion. In another patient, LA roof block was incomplete because of a vagal reaction during LA roof ablation with no further attempts of LA roof ablation. In the remaining 3 patients, a 80–100-ms conduction delay across the LA roof was observed despite application of up to 7 freezes. Owing to the learning curve associated with this method, the number of freezes decreased from 6 (4/7) in 2013 to 4 (3/4) in 2017 ($P = 0.007$).

3.2. Complications

One patient (0.9%) experienced PNP, owing to a too distal positioning of the CB in the right superior PV. Phrenic nerve function was recovered within 3 months. Another patient developed a postprocedural femoral artery hematoma with pseudoaneurysm necessitating (successful) surgical treatment. No atrioesophageal fistulas, thromboembolic events, or deaths were observed. No PNP occurred during LA roof ablation.

3.3. Midterm follow-up

During a median follow-up of 31 (IQR 11/44) months, LA roof ablation plus PVI restored and maintained SR in 78 (72.9%) patients (Fig. 2A) with recurrences in 29 patients (AF in 24; atrial tachycardia in 5). Electrical cardioversion during follow-up was performed in 8 (7.5%) patients. A dual-chamber pacemaker system was implanted in one patient with sick sinus syndrome. After the blanking period, 13 (12.2%) patients with

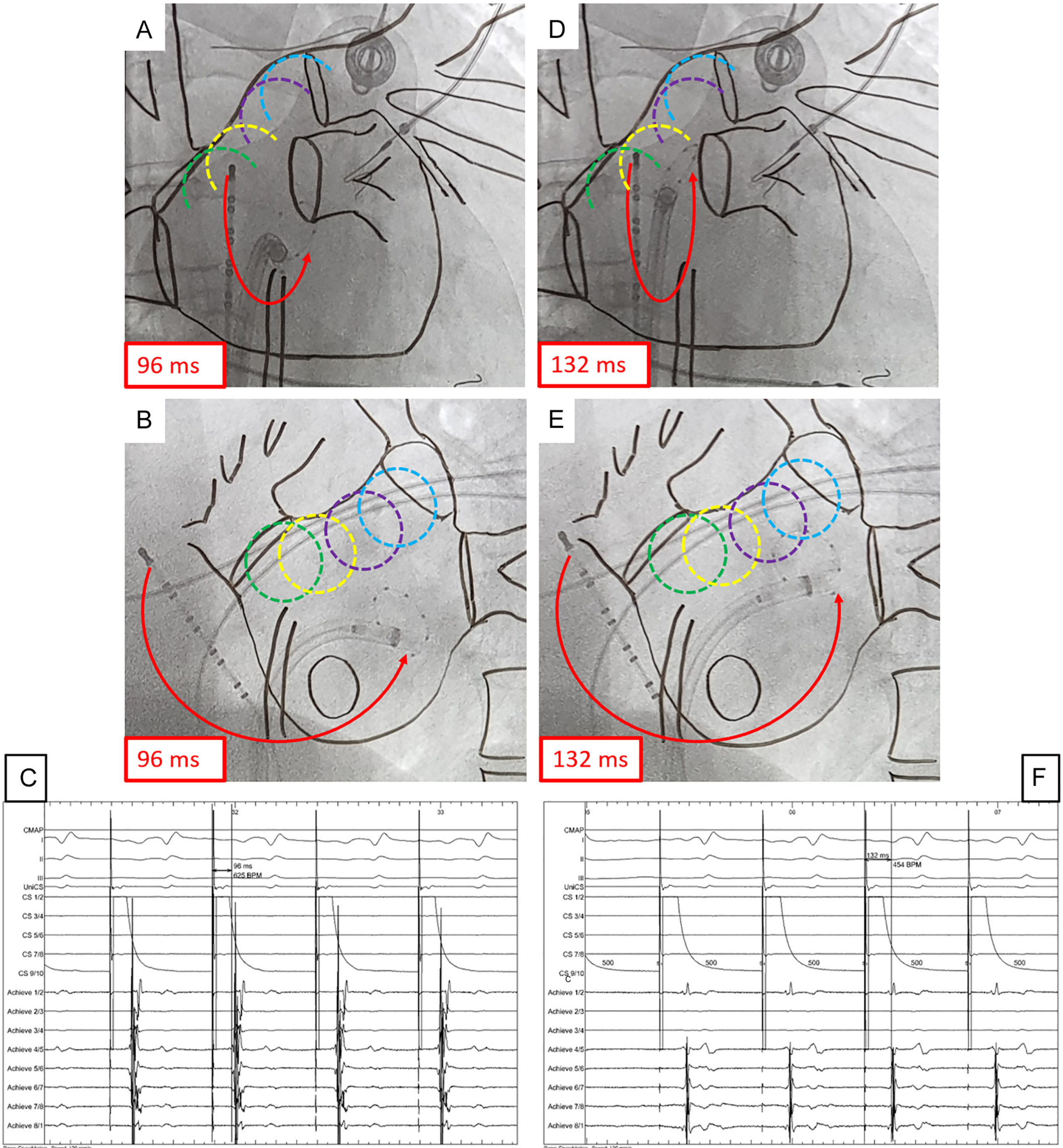

Fig. 1. A–F. Representative case of a caudocranial activation of the posterior LA wall after LA roof ablation using the second-generation CB (A + D: RAO 30° and B + C: LAO 60°). The LA and PV borders including the PV ostia and transseptal puncture site (determined by PV angiography) are marked with a dark line on the monitor screen. The [semi]circles (blue-purple-yellow-green dotted lines) represent balloon positions during ablation of the LA roof. The red ellipsoidal line shows the activation of the LA ("Achieve" catheter) during baseline pacing at the right atrial upper septum (decapolar "CS" catheter). Activation times increased form the caudal (96 ms) to the cranial position (132 ms) of the posterior LA wall next to the LA roof and verified a caudocranial activation. Abbreviations: CB, cryoballoon; CS, coronary sinus; LA, left atrial; LAO, left anterior oblique; PV, pulmonary vein; RAO, right anterior oblique.

symptomatic recurrences received AADs: flecainide (9 [8.4%]), amiodarone (2 [1.9%]) and dronedarone (2 [1.9%]). One patient on AADs during follow-up underwent repeat ablation. No late or unexpected complications were detected during follow-up.

Among the 29 patients with AFLAT recurrence, 10 (34.5%) underwent a repeat procedure using three-dimensional mapping technology (mean time between index and repeat procedures, 14 [IQR 25/75 5/19] months) (Table 3). LA roof conduction was recovered in 6/10 (60%) patients.

Table 1
Baseline clinical and demographic characteristics of all patients.

Variable	Entire cohort $n = 107$
Age, years (IQR)	62 (55/69)
AAD therapy before ablation	66 (61.7)
Female sex, *n* (%)	28 (26.2)
Hypertension, *n* (%)	80 (74.8)
Diabetes, *n* (%)	24 (22.4)
Coronary artery disease, *n* (%)	13 (12.2)
History of stroke, *n* (%)	2 (1.9)
History of TIA, *n* (%)	4 (3.7)
History of persistent AF since diagnosis, years (IQR)	1.9 (0.6/5.0)
LVEF, % (IQR)	60 (55/62)
CHA_2DS_2-VASc score, mean ± SD	1.8 ± 1.4
BMI, kg/m^2 (IQR)	27.4 (24.9/30.5)
GFR, ml/min/1.7 m^2 (IQR)	88.4 (75.1/101.9)
LA area, cm^2 (IQR)	24.6 (20.9/27.8)
LA area > 20 cm^2, *n* (%)	87 (81.3)
LA diameter, mm (IQR)	42 (39/45)
LA maximum volume, ml/m^2 (IQR)	39.4 (32.9/46.6)
LA minimum volume, ml/m^2 (IQR)	22.3 (15.6/27.0)
LA pre-systolic volume, ml/m^2 (IQR)	28.7 (21.8/33.9)
LAEF, % (IQR)	44.1 (34.2/52.4)
LAAEF, % (IQR)	21.2 (13.7/31.6)
LAPEF, % (IQR)	25.6 (18.7/32.6)
LAEI, % (IQR)	78.9 (51.9/110.2)

Abbreviations: AAD, antiarrhythmic drug; AF, atrial fibrillation; BMI, body mass index; GFR, glomerular filtration rate; IQR, interquartile range 25/75; LA, left atrial; LAEF, LA emptying fraction; LAAEF, LA active emptying fraction; LAEI, LA expansion index; LAPEF, LA passive emptying fraction; LVEF, left ventricular ejection fraction; SD, standard deviation; TIA, transient ischemic attack. Values are expressed as *n* (%), means ± SD, or medians (25th and 75th percentiles).

PV reconnections occurred in 7/40 (17.5%) veins in 5/10 patients. Low-voltage-area-guided RF ablation was performed in 3 patients (low-voltage areas occurred at the inferoseptal bottom of the LA (patient number 5 and 7) and the anterior aspect of the LA (patient number 6), respectively).

3.4. LA function after catheter ablation

Data from patients ($n = 60$) who underwent LA function analysis during stable SR before and 3 months after ablation were analyzed. There was no significant difference between the heart rates before and 3 months after ablation (66 [61/74]/min vs 69 [58/84]/min, $P = 0.51$).

Table 2
Procedural characteristics of all patients.

Variable	Entire cohort $n = 107$
Right atrial isthmus ablation, *n* (%)	5 (4.7)
Procedure time, min (IQR)	116 (9/126)
Fluoroscopy time, min (IQR)	20 (15/26)
Successful PVI, % of PVs	100%
Successful LA roof ablation, *n* (%)	98/107 (91.6)
Single-shot PV isolation, *n* (% of all PVs)	375/430 (87.2)
Number of freezes, *n* (IQR)	
PVs	8 (6/9)
LA roof	4 (3/6)
Bonus PV freezes, *n* (%)	67 (62.6)
Cryoenergy application time (IQR)	
All PVs, min	24 (19/29)
LA roof, sec	720 (540/975)
Nadir temperature, −°C (IQR)	
PVs	49 (45/53)
LA roof	40 (37/43)
Conduction delay, ms (IQR)	140 (128/159)
RF-based touch-up lesions, *n*	0

Abbreviations: IQR, interquartile range; N/A, not assessable; LA, left atrial; PV, pulmonary vein; PVI, pulmonary vein isolation; RF, radiofrequency. Values are expressed as *n* (%) and medians (25th and 75th percentiles).

Maximum, minimum, and pre-systolic LAVs were higher at baseline than at the 3-month follow-up (maximum LAV, 39.4 [32.9/46.6] vs. 34.2 [26.8/41.2] ml/m^2, $P < 0.01$; pre-systolic LAV, 28.7 [21.8/33.9] vs. 25.6 [19.2/30.7] ml/m^2, $P = 0.02$; minimum LAV 22.3 [15.60/27.0] vs. 17.4 [13.1/23.4] ml/m^2, $P < 0.01$) (Fig. 2B).

In contrast, baseline LAEF did not differ from LAEF at the 3-month follow-up (44.1% [34.2/52.4] vs. 47.4% [38.5/55.8], $P = 0.25$). Similar results were obtained for LAPEF (25.6% [18.7/32.5] vs. 22.1% [15.8/31.3], $P = 0.11$) and LAEI (78.9% [51.9/110.2] vs. 90.1% [62.5/126.0], $P = 0.32$), whereas LAAEF significantly increased (21.2% [13.7/31.6] vs. 29.1% [23.1/36.0], $P < 0.01$). However, at 3 months, LAEF was significantly higher in successfully ablated patients than in patients who experienced AFLAT recurrences during further follow-up (48.3% [40.1/55.7] vs. 35.4% [32.3/52.2], $P < 0.01$).

4. Discussion

4.1. Major findings

To our knowledge, this is the first analysis of midterm outcome and LA function after CB-Adv PVI plus LA roof ablation in persistent AF patients [1]. The acute success rate for PVI plus LA roof ablation was 91.6% [2]. PVI plus LA roof ablation showed a promising midterm outcome (72.9% AFLAT-free survival) after a single procedure and may be safe and effective for persistent AF patients without impairing total LA function until the 3-month follow-up [3]. Operator experience gradually improved, as evidenced by a continuous yearly decrease in fluoroscopy and procedure times.

4.2. Safety

Acute procedural complications associated with CB ablation of persistent AF patients are reported in up to 6% of cases [13–16]. Our overall complication rate (1.8%) falls within this range Collateral tissue damage near the posterior LA wall, including the phrenic nerve, is a risk with any technology that creates wider lesions. Improved ablation and monitoring techniques seem to lower the risk of phrenic nerve injury [10]. PNP occurred in one patient and was associated with PV isolation. We observed no phrenic nerve injuries during LA roof ablation. Furthermore, there were no atrioesophageal fistulas in our cohort. Five cases of atrioesophageal fistula formation with CB ablation have been reported [17,18] all of which were related to the left inferior PV [19]. LA roof ablation between the upper PVs seems unlikely to be associated with a significantly increased risk of atrioesophageal fistulas.

4.3. Midterm outcome

Circumferential PVI with verification of electrical isolation, both with and without additional linear lesions [6,7,13–16], probably represents the most accepted ablation strategy for persistent AF patients undergoing the first ablation procedure. Despite the various ablation strategies available, the single-procedure efficacy of CB or RF PVI alone in persistent AF patients is limited, particularly when outcomes of >1 year are considered: short- to midterm (median follow-up, ≤22 months) success rates of up to 67% were achieved after PVI alone [13,15,16]. In our study (median follow-up, 31 months), the single-procedure clinical success rate after CB PVI plus LA roof ablation was relatively high (72.9%) and better than that in a recent study in our center [14] involving a historical cohort of 281 persistent AF patients undergoing CB PVI only (63.3% arrhythmia-free survival; median follow-up, 33 months). A matched cohort of these two groups show a higher arrhythmia-free survival after PVI plus LA roof ablation compared to PVI only, see supplementary online data (Supplementary Table 4 and Supplementary Fig. 3). Nevertheless, this should be the subject of a further continuation of this trial.

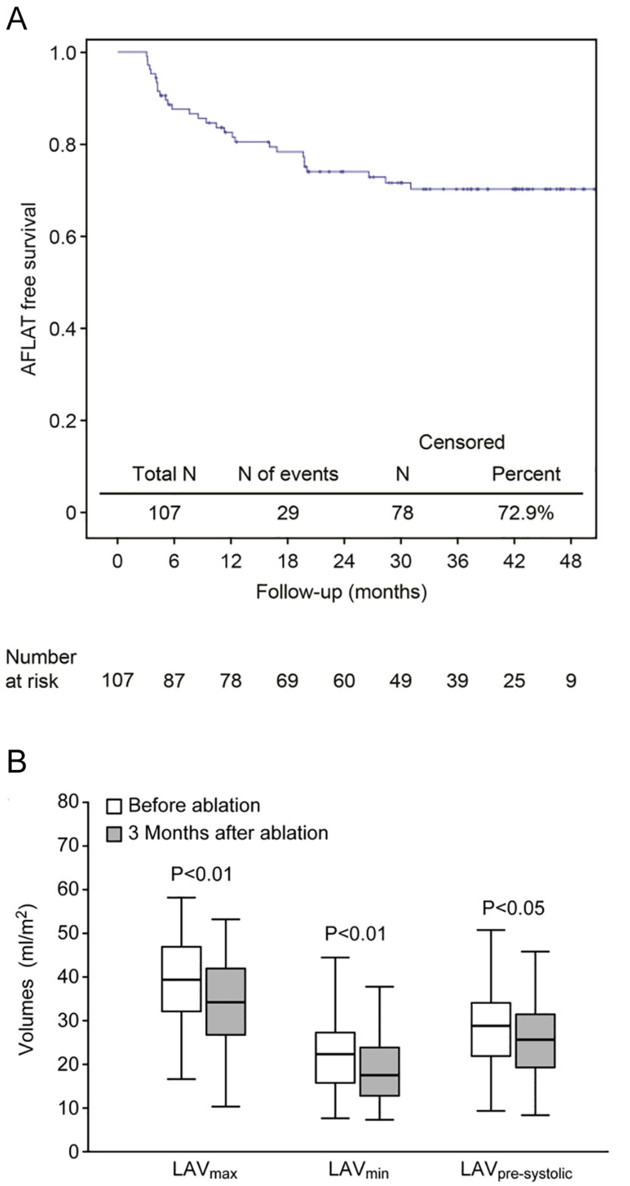

Fig. 2. (A) Kaplan-Meier analysis of AFLAT-free survival after a single ablation procedure in the entire cohort. (B) Changes of phasic volumes during 3-month follow-up according to baseline LAV_{max}, LAV_{min} and $LAV_{pre-systolic}$. Abbreviations: AFLAT, atrial fibrillation, atrial flutter, or atrial tachycardia; LAV, left atrial volume.

Table 3
Redo procedures with the according ablation strategies.

Patient number	Indication for redo procedure	PV reisolation				RL	ML	LVA	Origin of AT
		LS	LI	RS	RI				
1	AT	+	+	+	−	+	−	−	Left superior PV
2	Persistent AF	−	+	−	−	−	−	−	
3	Persistent AF	+	−	−	−	+	−	−	
4	AT	−	−	+	−	+	−	−	Anterior aspect of LAA
5	Persistent AF	−	−	−	−	+	−	+	
6	Persistent AF	−	−	−	−	−	−	+	
7	AT	−	−	−	−	−	−	+	Right atrium posteroseptal
8	Persistent AF	−	−	−	−	+	−	−	
9	AT	−	−	−	+	−	−	−	Right superior PV
10	AT	−	−	−	−	+	+	−	Perimitral

Abbreviations: AF, atrial fibrillation; AT, atrial tachycardia; LAA, left atrial appendage; LI, left inferior; LS, left superior; LVA, low-voltage area; ML, mitral line; PV, pulmonary vein; RI right inferior; RL, roof line; RS, right superior.

4.4. Rationale for LA roof ablation using cryoenergy

Because ablation efficacy seems to be related to ablated tissue extent, the trend has been toward using more-extensive ablation [6,7]. By creating contiguous lesions with the CB-Adv in addition to PVI, LA roof ablation with posterior orientation can further modify the substrate between the upper PVs [8]. The improvements of the CB-Adv over its predecessor have led to a more uniform freezing zone and homogeneous cooling of the entire distal balloon hemisphere, resulting in increased effectiveness and better clinical outcomes [2]. In particular, the wider freezing area extending from the distal portion to the equator of the balloon allows linear lesions generation [20]. The CB-Adv may create larger areas with more-homogeneous substrate modification (also at the LA roof and the posterosuperior wall) and thus fewer areas of arrhythmogenesis due to incompletely ablated tissue or incomplete lines of conduction block, as described previously for point-by-point RF ablation resulting in LA tachycardias [21]. Another recent study found that the low-voltage areas attained with the CB are significantly larger and the unexcitable tissue along the ablation lines is much wider than with RF ablation [22]. Furthermore, as suggested previously [23], ablative LA debulking can improve long-term efficacy by reducing the intact posterior wall. The use of CB-Adv for LA roof ablation builds on this debulking potential.

Despite our success, LA roof ablation can be challenging and time consuming, and the resulting scar tissue can cause LA tachycardias due to incomplete lines, at least when the RF technique is used [21]. Further electrophysiological studies after LA roof ablation using a CB must be performed to determine whether the LA roof gap rate increases and to determine the role of roof line conduction recovery, as described for RF ablation [21]. Maybe that the debulking caused by consecutive CB ablations along the LA roof and posterosuperior wall in our trial is the actual benefit as roof dependent atrial tachycardias were not described in patients with recurrences.

The LA roof conduction recovery rate (60%) was comparable to that reported for RF ablation [24]. However, this rate is based only on the 34.5% of patients with arrhythmia recurrences who underwent a repeat procedure. The modest number of repeat ablations prevents free extrapolation to all patients with arrhythmia recurrences. Furthermore, we cannot exclude the impact of the learning curve, because all patients with LA roof conduction recovery were among the first 40 patients undergoing the index procedure during 2013–2014.

4.5. LA roof ablation: who benefits most?

Evidence for the efficacy of LA roof ablation as a common strategy in persistent or permanent AF patients is inconclusive. Trials and meta-analyses [25,26] have demonstrated significant advantages of PVI plus linear ablation. In contrast, the randomized STAR-AF II trial [16] showed that neither linear ablation nor ablation of complex fractionated electrograms in addition to RF PVI reduces AF recurrence rates. However, in studies of persistent AF patients [26], there is evidence of significant heterogeneity in line type, AAD use, blanking period duration, intensity of follow-up monitoring, and specific population characteristics, and this heterogeneity may be related to the different outcomes. In this context, we must point out that CB-Adv lesions could more accurately be described as an "area" of the LA roof and upper posterosuperior wall than as a "line". This fact should be seen against the background of the controversy regarding the benefit of additional linear ablation, in consideration of the STAR-AF II trial. Furthermore, a recent comparison of PVI alone with PVI plus posterior wall ablation (both using the CB technique) suggests that the latter is superior [27].

Determining who may benefit from additional procedural approaches is important. Additional linear lesions along the LA roof may be especially beneficial in patients with a steeply angled LA roof, large left atrium, or closely spaced septal and lateral PV areas (and thus upper veins) at the LA roof [28,29]. Although CB-Adv PVI is effective and leads to both PVI and LA substrate modification surrounding the

PV areas, PVI alone might be insufficient in patients with LA enlargement, owing to the larger residual substrate areas. An additional LA roof ablation using CB-Adv may improve outcomes over PVI alone, especially in patients with LA enlargement, as reported previously in a study comparing the CB and RF techniques [30].

Nevertheless, randomized trials (PVI alone vs. PVI plus LA roof ablation) with preprocedural imaging tools are needed to determine who will benefit from additional LA roof ablation using a CB. Furthermore, a completely "debulking" of the posterior wall as described by Aryana et al. [27] should be compared to LA roof ablation including preprocedural imaging. Most likely, prolonged procedure and fluoroscopy times as well as the higher risk of atrioesophageal fistula during posterior wall ablation must be taken into consideration.

4.6. Does LA roof ablation affect LA function?

Conflicting data on LA function recovery after ablation can be attributed mainly to differences in imaging techniques (echocardiography, MRI, or computed tomography), parameters for assessing LA function, and timelines for LA function evaluation [31,32]. The criteria for echocardiographic evaluation of LA function are not standardized, given that different methods have been used to assess LA function in research and in clinical practice. Comparing data collected at different times before and after ablation should, however, compensate for biases intrinsic to a specific approach. The LA serves multiple functions (reservoir during LV systole, conduit for blood transiting during early diastole, and active contractile pump in late diastole).

Among the many available parameters for assessing LA performance, we chose LAEF, calculated as the ratio between LAVs during different cardiac cycle phases. Atrial volume measurements obtained by different imaging techniques are not superimposable [33]. The use of a ratio of the same volume at different cardiac phases, measured by the same operator, can help to overcome this mismatch and make LAEF an optimal marker of atrial function, being similar to markers calculated using MRI, the gold standard for assessing LA dimensions and function [34].

In our trial, PVI plus LA roof ablation led to a postprocedural decrease of LAVs with no significant change in or only a slight increase in LAEF, which is consistent with the results of a recent meta-analysis [31]. There appears to be a significant difference in LAEF between arrhythmia-free patients and patients with arrhythmia recurrences during follow-up after catheter ablation of persistent AF patients [32]. Abhayaratna et al. described even a predictive value of LAEF for atrial arrhythmias in 574 elderly patients. Among these, patients with AF or atrial flutter had a lower LA reservoir function, as detected by LAEF [35]. The measurement of LAEF 3 months after ablation in our trial maybe a possible way to detect patients, who benefit from PVI plus LA roof ablation during further follow-up. Nevertheless, the short follow-up duration in our study of LA function must be considered.

Changes in LA function after ablation depend on the balance between the benefits of atrial remodeling and the harmful effects of edema and fibrosis, a balance that may lead to fluctuations in LA function. Although PVI plus LA roof ablation using a CB appeared not to substantially impair LA function, the beginning and the impact of scar tissue on atrial performance is unclear. As demonstrated previously, extensive LA scarring due to ablation impairs LA function (as evaluated by MRI) [36]. The extent to which this may be transferable to LA roof ablation with a CB should be studied further, with a longer follow-up and MRI assessment of LA scarring.

Finally, the impacts of LA roof ablation with a CB on blood stasis within the LA and on the associated thromboembolic risk are unclear. We observed no concrete indications of thromboembolic events. The thrombus formation risk may not be increased, perhaps because LA function was preserved after LA roof ablation. Nevertheless, further evaluation using cranial MRI after LA roof ablation would be reasonable.

4.7. Study limitations

This nonrandomized study without a direct comparison to patients undergoing PVI alone suffers from the limitations of the retrospective study design and inherent selection bias. In addition, we did not consider recurrence during the blanking period, which could lead to overestimation of the true success rate; and intermittent rhythm monitoring may be inferior to continuous monitoring with implanted devices, especially in asymptomatic patients. Additionally, our cohort is too small to estimate the probability of atrioesophageal fistula after multiple freezes at the superior posterior wall during LA roof ablation. Final conclusions regarding the safety profile requires additional research. Furthermore, two-dimensional echocardiography has some limitations in assessing LA volume, mainly due to difficulty in endocardial border tracing and the fact that it relies on geometrical assumptions that ignore LA geometry differences between individuals. LA volumes estimated by 2-D echocardiography are lower than LA volumes estimated by MRI, which is now considered to be the gold standard for assessment of LA dimension and function. In addition, the LA appendage was not evaluated after ablation. Although complete LA appendage assessment prior to ablation is mandatory to avoid atrial thrombosis, transesophageal echocardiography is an invasive technique with possible complications. Therefore, it is unsurprising that transesophageal echocardiography for all patients during follow-up was not carried out. Finally, in previous studies, LA function analysis was performed both during AF and sinus rhythm. The occurrence of AF during echocardiography was among the exclusion criteria for the present study. If one LA image was acquired during AF and another in SR, variation of minimum LA volume, in particular, might be underestimated. Moreover, it would be impossible to perform an ECG-based analysis of presystolic phasic volumes. Thus, the conclusions regarding LA function are limited to only those patients in sinus rhythm before and a short-term period of 3 months after ablation.

5. Conclusions

PVI plus LA roof ablation with the CB-Adv is safe and shows a promising midterm outcome without impairing LA function within a 3-month follow-up. Thus, this adjuvant treatment may be an option for persistent AF patients in centers highly experienced in the CB technique. Nevertheless, our results must be confirmed in a prospective randomized trial before LA roof ablation using the CB-Adv technique can be recommended in clinical guidelines.

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Conflicts of interest

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