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ATRIAL FIBRILLATION CRYOBALLOON ABLATION IN PATIENTS WITH A COMMON PULMONARY VEIN TRUNK

K.V.Davtyan, A.H.Topchyan, A.A.Kalemberg, G.Yu.Simonyan

National Medical Research Center for Preventive Medicine, 101000, Petroverigskiy lane 10-3, Moscow, Russia

Objective: we aimed to assess the efficacy and safety of pulmonary vein (PV) cryoballoon ablation (CBA) in patients with a common trunk of the pulmonary veins (PVCT).

Materials and methods: We performed a retrospective analysis of 596 primary PV CBA procedures using the second-generation cryoballoon (CB) Arctic Front Advance (28 mm). PV anatomy was visualized using direct LA angiography during high-frequency right ventricular pacing. We included forty-nine patients in whom a PVCT was identified. The one-step and sequential ablation approaches with simultaneous recording of biophysical and electrophysiological parameters were used for PVCT isolation. During CBA in the right PVs, high-output (2000 ms, 25 mA) pacing of the right phrenic nerve was performed via a electrode placed in the superior vena cava, and amplitude of diaphragm movement was monitored. In the case of impairment/loss of the diaphragm contraction ablation was immediately stopped.

Results: 91.1% (543) patients had the normal drainage of PV. In 4 patients (0.67%), an additional right pulmonary vein was identified. The prevalence of PVCT was 8.2% (49 pts): a left common trunk (LCT) was observed in 43 patients (87.7%), a right common trunk (RCT) - in 6 patients (12.2%). Acute efficacy of PVCT isolation was 95.9% (47/79): in LCT - 95.3%, in RCT - 100%. The feasibility of the one-step antral isolation was 59.1% (n=29). During a median follow up of 12 (3-20) months, the clinical success rate of the procedure was 69.4%. A comparative analysis showed no significant difference between common trunk ablation approaches and clinical efficacy (p=0.346).

Conclusion: CBA has been shown effective and safe for symptomatic AF patients with PVCT. The simultaneous and sequential ablation approaches can be performed with comparable efficacy.

Keywords: atrial fibrillation, catheter isolation; cryoballoon ablation; pulmonary veins common trunk

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Corresponding author: Davtyan Karapet, E-mail: doctordavtyan@mail.ru

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Pulmonary vein isolation (PVI) with catheter ablation is the first-line therapy of symptomatic, antiarrhythmic drug (AAD) resistant atrial fibrillation (AF), including patients with variable anatomy of the pulmonary veins (PV) [1-3]. PV cryoballoon ablation (CBA) is a new option of the single-shot PVI [4, 5]. The comparable efficacy and safety of CBA to radiofrequency ablation (RFA) and steep learning curve have led to the widespread adoption of the cryoballoon technology [6, 4]. On the first view, CBA seems to be more dependent on PV anatomy, than RFA. The pattern of PV drainage, in particular, the presence of the common trunk, the length of the common trunk, PV ostium shape and size may compromise the contact stability between the cryocatheter and tissue, hence the PVI efficacy. The PV drainage pattern of with common trunk is more frequent on the left (8-32%). The additional PV is common on the right (16-35%) [8-12]. This study aimed to assess the safety and efficacy of the PV CBA in patients with the pulmonary vein common trunk (PVCT).

MATERIAL AND METHODS

We have performed a retrospective analysis on the procedural data of the five hundred and ninety-six PV CBA using the second-generation cryoballoon Arctic Front Advance (28 mm, Medtronic) in patients with drug-resistant, paroxysmal/persistent AF. The patients consequently underwent the primary PV CBA between November 2016 and November 2018 in National medical research centre

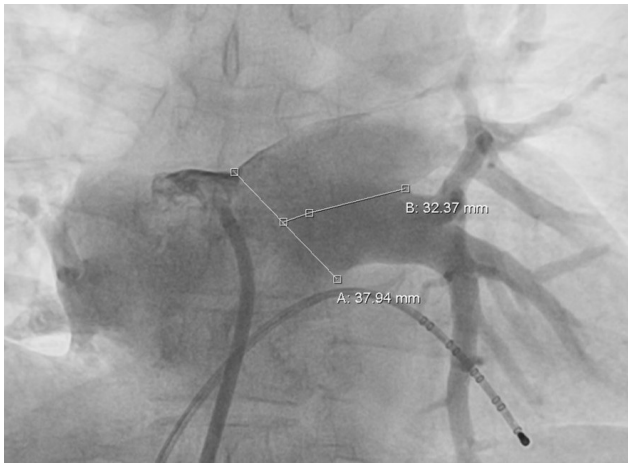

Figure 1. Angiography of the left atrium and pulmonary veins. The large and long pulmonary venous trunk is a limitation for cryoballoon ablation.

for preventive medicine. PV anatomy was visualised using a direct LA angiography on high-frequency right ventricular pacing. The evaluation of both large (≥26 mm) and long (≥10 mm) PVCT in three patients limited CBA performance (fig. 1). We enrolled forty-nine patients (8,2%) with evaluated PVCTs in the study. The minimum PVCT length was set to five mm.

Patients' clinico-demographic characteristics

The patients' median age was 61 yrs (interquartile range (IQR) 53-67), 49% (n=24) were females. The median age at the time of arrhythmia manifestation was 56 (50-62) yrs. The majority of the patients (91.8%) had paroxysmal AF with a median duration of AF history of 2 (1-5) years. The mean left atrium (LA) size was 40.5±4.6 mm, and the mean left ventricular ejection fraction 62.9±5.4%. The most frequent comorbidity was arterial hypertension (67.3%). Two patients (4.1%) had diabetes mellitus. The median CHA_2DS_2-VASc score was 1 (1-2).

Pulmonary vein cryoballoon ablation

The PV CBA was carried out under continuous intravenous sedation with propofol. The transseptal puncture was performed in the fossa ovalis under the intracardiac echocardiography (ICE) (Vivid I Safelock Cart, GE Healthcare, AcuNav 10-French, Siemens AG, Germany) using an 8 Fr. transseptal sheath (SR0, St. Jude Medical) with Brockenbrough needle. Intravenous heparin was administered

Table 1.
The set of cryoballoon isolation parameters, registered online during the procedure

CBA parameter		LSPV	LIPV	RIPV	RSPV
PV activity on Achieve catheter		yes	yes	no	yes
Applications number		1	1	1	1
Applications duration, sec.		240	240	240	240
Time to PVI, sec.	Entrance block	45	38	-	52
	Exit block	-	-	28	-
PV occlusion stability on the 30-th sec.		yes	yes	yes	yes
Cryoballon minimum temperature,°C		-46	-44	-51	-50
Acute PVI		yes	yes	yes	yes

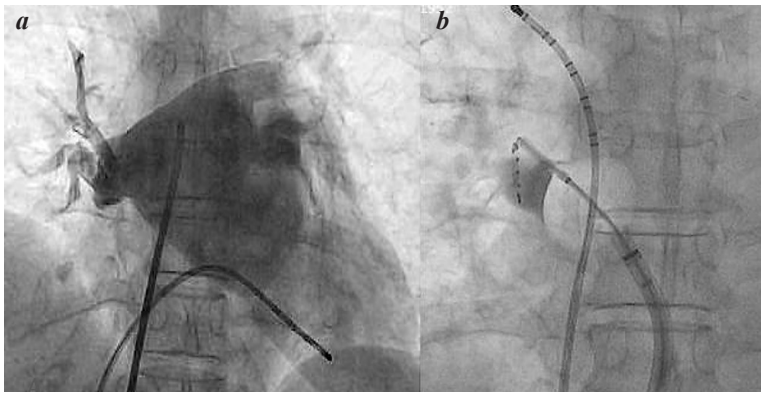

Figure 2. One-step cryoballoon ablation of the pulmonary veins' common trunk a) the visualisation of the right common pulmonary vein trunk on the left atrial angiogram, b) complete occlusion of the trunk by second-generation cryoballoon Arctic Front advance. We observed atrial fibrillation episode termination at the time of the right trunk isolation.

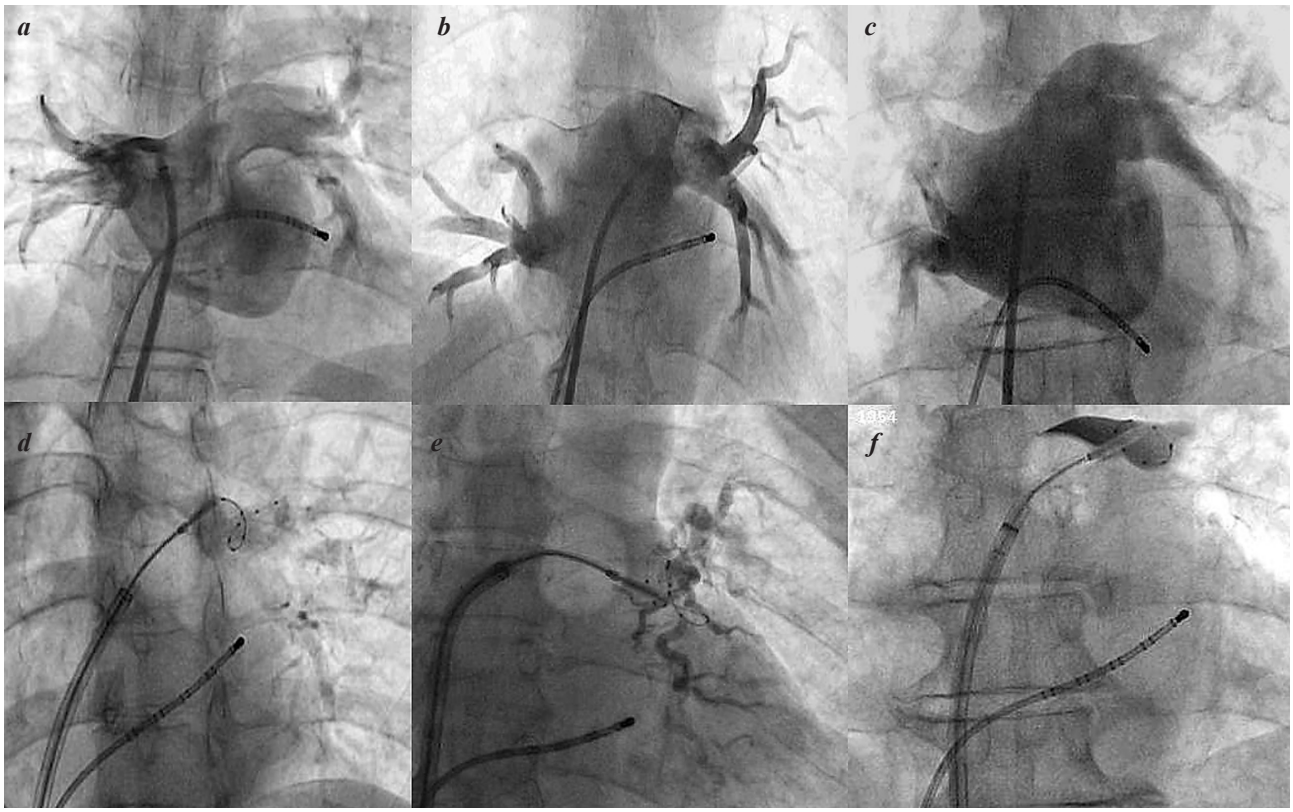

Figure 3. The variability of the left common trunk anatomy (a-c) and cryoballoon ablation approaches (d-f).

at the time of transseptal puncture (target activated clotting time ≥250 s) to prevent thromboembolic events. A decapolar diagnostic catheter (Webster Decapolar Deflectable Catheter, Biosense Webster, USA) was inserted into the right ventricle (RV). We performed a high rate RV pacing (cycle length 250 ms, MicroPace EPS 320, Micropace Inc., USA) to enhance the quality of LA anatomy visualisation. After LA angiography, we placed the diagnostic catheter into the coronary sinus (CS). The minimum length of the common trunk between common ostium and first branching was set to five mm. If no limitations for CBA were observed, the transseptal sheath was exchanged to cryoballoon delivery system FlexCath (Medtronic, USA, 12 Fr). The second-generation cryoballoon Arctic Front Advance with Achieve diagnostic catheter (Medtronic, USA) was advanced via the delivery system to the LA. The Achieve catheter was positioned to the PV ostium to map venous electrical activity. Then the catheter was inserted distally into the PV to support cryoballoon positioning. The cryoballoon was inflated in the PV and advanced to the PV ostium. PV angiography was performed to confirm the complete PV occlusion by the cryoballoon. We performed CBA in the clockwise direction (left superior PV, left inferior PV, right inferior PV, right superior PV). Initially, the application duration was 240 sec. Since March 2018, we have reduced the application duration to 180sec based on the results from the growing number of publications on efficacy and safety of shorter cryoapplication duration [13-15]. Ten patients underwent CBA with the application duration of 180sec. For PVCT isolation, we have used both one-step and sequential ablation approaches. If necessary additional applications were performed to complete PVI. Table 1 presents the example of CBA parameters set, registering during each PVI procedure.

We monitored diaphragmatic contraction by abdominal palpation during right phrenic nerve pacing (30 bpm, 24 mA) while performing CBA in the right PVs. In the case of diaphragm contraction weakening or disappearing the freezing was immediately discontinued, and the cryoballoon was deflated.

We have continuously monitored PV activity on Achieve catheter to verify PVI in real-time. If we could detect no PV activity, we paced the Achieve catheter (the dipole with stable conduction to LA) to verify the exit block. When necessary, we used the independent two-channel pacing in the right PVs to assess right phrenic nerve function and verify the exit block. After completing CBA, we remapped each PV and confirmed the exit block. In doubtful cases of LA capture, while pacing PV, we placed the decapolar diagnostic catheter on the possible closest part of the atrial myocardium to the paced PV. In the cases of atrial capture, the delay between stimulus artefact and atrial capture on the decapolar catheter was minimal (≤30 ms).

Postprocedural management

The patents restarted antithrombotic therapy in four hours after control echocardiography excluding pericardial effusion. Antiarrhythmic drugs for 3-6 months had been administered to five patients with persistent AF. Patients with paroxysmal AF did get no antiarrhythmic therapy. We have assessed the procedure clinical efficacy using results of rest ECG, 24-hours Holter monitoring and telephone survey, performed in 3, 6, 12 months after the procedure.

Statistical analysis

We performed statistical analysis using Microsoft Excel 2016 (Microsoft Corporation, USA) and SPSS for Windows (IBM Corporation, USA). Normality was assessed using the Shapiro-Wilk test. Continuous variables were presented as mean ± standard deviation (SD) median (Me) and interquartile range (IQR). Comparisons between two groups were performed with the Mann Whitney U test and Student's T-test, as appropriate. We used Pearson's chi-squared test for categorical variables. A two-tailed p-value ≤ 0.05 was regarded to be significant.

Table 2.

Comparative characteristics of PV common trunk ablation approaches

	Approach subgroup		P value
	One-step ablation	Sequential ablation	
PVCT number, n	29	20	-
Applications per vein, n	1.33	1.16	0.051
Applications duration, sec.	296.5	274.5	0.543
PVI in real time, %	64.4%	63.2%	0.878
PV complete occlusion by cryoballoon, %	88.75	91.5	0.566
Cryoballoon minimal temperature, ºC	49.6	49.3	0.813

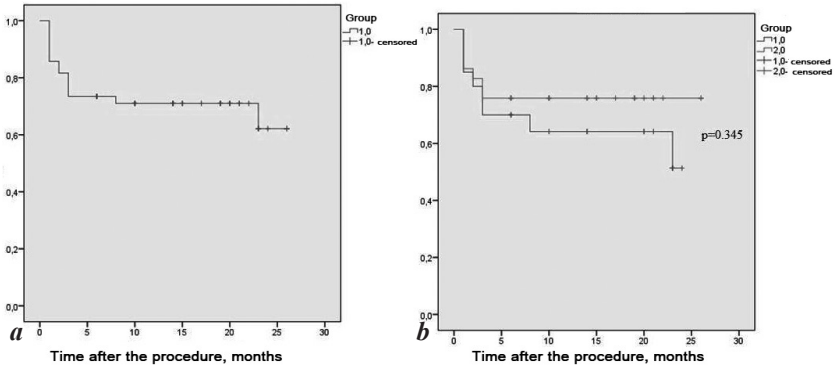

Figure 4. Clinical efficacy of cryoballoon ablation in patients with pulmonary veins' common trunk a) in the study population, b) in the subgroups of one-step and sequential ablation approaches (group 1 - sequential ablation, group 2 - one-step ablation).

RESULTS

Five hundred forty-three patients (91.1%) had the typical pattern of PV drainage (four PV ostia on the LA posterior wall). Four patients (0.67%) had an additional right PV (right middle PV). Forty-nine patients (8.2%) had a common PV trunk. Forty-three from forty-nine (87.7%) had a left common trunk, six patients (12,2%) - right common trunk. Procedural PVI success rate was 98.6%. We successfully isolated 95.9% (47 from 49) PV trunks and

100% right PVs. We performed one-step cryoablation in twenty-nine common trunks (59%) (fig. 2). For twenty PV trunks (41%), we used the sequential ablation approach (fig. 3. e-f).

The total number of PVI, using second-generation cryoballoon, was 147. The number of cryoapplication per vein was 1.4, application duration per vein - 284.2 sec. The complete PV occlusion by cryoballoon was achieved in 89.9% PV. The minimal cryoballoon temperature was 48.6±6.5ºC. Online PVI verification was possible in 64.9% PV; the median time to PVI was 42 (28-55) sec. Right phrenic nerve injury occurred in no patients. One patient (2.04%) developed a right femoral vein access site haematoma, managed surgically.

Table 2 presents the comparative analysis of procedural characteristics depending on the common trunk ablation approach (one-step and sequential). As the table shows, the ablation approach had no implications for biophysical and electrophysiological parameters of CBA.

Complications

One patient (2.04%) developed a large right femoral haematoma, requiring surgical intervention.

Clinical efficacy of the procedure

The procedure success rate (sinus rhythm maintenance) was 69.4% at the median follow-up time of 12 (3-20) months (fig. 4a). Fig. 4b presents the Kaplan-Meier curve of PVCT two ablation strategies, showing comparable efficacy of one-shot and sequential ablation strategies for PVCT (p=0.345).

DISCUSSION

Our study confirmed the high efficacy and safety of CBA in patients with PVCT. The freedom from arrhythmia was 69.4%, which correlated well with data from other trials [12,16].

Heeger et al. reported the comparable procedural and clinical success rate in patients with left common trunk and typical PV drainage pattern. The frequency of left common trunk, in this study, conducted in three high-volume centres, was 11%. All common trunks (100%) were successfully isolated. There were no statistical differences in applications per vein, time to PVI, cryoballoon minimum temperature between the groups. Khoueiry et al. demonstrated comparable clinical efficacy of CBA and RFA in patients with paroxysmal AF and variable PV anatomy [12]. The study, conducted by Tsyganov et al. [17], confirmed the universality of ballon technologies in variable PV anatomy. PVCT was not a predictor, too in the study, conducted by Huang et al. [18]. However, Chichkova et al. reported, that PVCT pattern was associated with higher procedure-related complications rate, in particular, pericarditis [19]. Indeed, the small sample size (n=7) suggests the sporadic character of the observed cases. Still, the authors' hypothesis of distally placed (outside the contour of the heart) cryoballoons damaging effect on epicardium seems to be logical. From this point of view, the strategy of our centre, limiting CBA in the cases of both large (>26 mm) and long (>10 mm) PVCT is justified in order to avoid such a grave complication as atrial-oesophagal fistula.

Interestingly the LA and PV computer tomography before catheter ablation has been performed rarer the recent years [16, 18]. Apart from the cost-efficacy, the growing experience of AF CA independent on PV anatomy is the possible explanation for this observation. Also, new mapping and ablation technologies have improved the feasibility of the catheter ablation. Probably that is the reason why data from the early studies, reporting catheter ablation dependence on PV anatomy, has not been confirmed in recent trials [11, 17, 20].

Nowadays, the main limitation to perform CBA is both large (≥26 mm) and long (>10 mm) PVCT (fig. 1). From this point of view, the results of the analysis of the three-dimensional PV ostium and antrum anatomy are impressive [21]. The distance between common ostium to first branching was 0-5 mm in forty-three patients from ninety-four (45.7%) and 5-15 mm in thirty-seven patients (39.4%). Only in fourteen patients (14.9%) the length of the common trunk was more than 15mm. Thus, the frequency of PVCT not feasible for CBA is low.

LIMITATIONS

The study is a retrospective analysis of the prospectively collected data. The likelihood of insufficient AF relapse evaluation, changes in cryoapplication duration (shift from 240 sec to 180 sec) are these study limitations. Further follow-up is necessary to assess the comparative procedure efficacy between patients with PVCT and typical PV drainage.

CONCLUSIONS

CBA of PVCT is efficient and safe in patients with symptomatic AF. One-shot and sequential ablation approaches can be used for PVCT isolation with comparable efficacy.

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