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RUSSIAN REGISTRY OF CRYOBALLON ABLATION OF ATRIAL FIBRILLATION: CHARACTERISTICS OF THE PROCEDURE AND FEATURES OF PATIENT'S MANAGEMENT

L.E.Korobchenko[1], T.A.Lyubimtseva[1], K.V.Davtyan[2], A.G.Topchyan[2], G.Yu.Simonyan[2], S.E.Serduk[2], S.V.Korolev[3], A.Ya.Kosonogov[4], K.A.Kosonogov[4], E.S.Tarasyuk[5], K.A.Lubenkov[5], A.S.Shulga[5], E.A.Artyukhina[6], A.Sh.Revishvili[6], D.V.Kryzhanovskii[7], R.E.Batalov[8], S.Yu.Usenkov[8], D.N.Khomutinin[9], G.V.Kolunin[9], V.E.Kharats[9], A.A.Nechepurenko[10], I.Sh.Sagitov[11], N.I.Grachev[12], N.L.Sharikov[13], S.Yu.Chetverikov[13], D.I.Perchatkin[14], Yu.V.Virstyuk[15], F.G.Rzaev[16], D.S.Lebedev[1], E.N.Mikhaylov[1]

[1]FSBI "Almazov NMRC" of the MH RF, 2nd Akkuratova str., Saint Petersburg, Russia; [2]FSBI "NMRC for Therapy and Preventive Medicine" of the MH RF, 10th Petroverigsky Lane, Moscow, Russia; [3]FSBI "Federal Scientific and Clinical Center for Specialized Types of Medical Care and Medical Technologies of the FMBA", Russia, Moscow, 28th Orekhovy Boulevard; [4]State budgetary medical centre "City Clinical Hospital N5" of the Nizhny Novgorod district of Nizhny Novgorod, Russia, Nizhny Novgorod, 34th Nesterova str.; [5]Federal state budgetary educational institution of higher education "Amur State Medical Academy" of the MH RF, Russia, Blagoveshchensk, 95th Gorky str.; [6]FSBI " Vishnevsky NMRC for Surgery" of the MH RF, Russia, Moscow, 27th Bolshaya Serpukhovskaya str.; [7]State budgetary medical centre "City Hospital N26" of St. Petersburg, Russia, St. Petersburg, 2nd Kostiusko str.; [8]Scientific Research Institute of Cardiology - branch of the FSBI "Tomsk National Research Medical Center of the RAS", Russia, Tomsk, 111-A Kievskaya str.; [9]State budgetary medical centre "Regional Clinical Hospital N1" of Tyumen region, Russia, Tyumen, 55th Kotovsky str.; [10]FSBI "Federal Center of Cardiovascular Surgery" of the MH RF, Astrakhan, 4th Pokrovskaya Grove str., [11]State budgetary medical centre "Republican Center of Cardiology" of the Republic of Bashkortostan, Russia, Ufa, 96th Stepan Kuvykin str.; [12]Primorsky Regional Clinical Hospital N1, Vladivostok, 53th Aleutskaya str., Russia; [13]Budgetary Institution "District Clinical Hospital" of Khanty-Mansiysk Autonomous Okrug-Yugra, Russia, Khanty-Mansiysk, Kalinina str., 40; [14]State budgetary medical centre "City Pokrovskaya Hospital" of Saint Petersburg, Russia, St. Petersburg, 85thBolshoy pr. VI; [15]Commercial Institution of Healyh "Russian Railway Company-medicine", Russia, Moscow, 2c4 Budayskaya str.,; [16]State budgetary medical centre "I.V.Davydovsky City Hospital", Russia, Moscow, 11th Yauzskaya str.

Aim. To study the characteristics of the atrial fibrillation (AF) cryoballoon ablation (CBA) procedure and features of patient's management in real clinical practice in Russia.

Methods. "Prospective Atrial Fibrillation Cryoablation Registry" is an observational prospective national multi-center study. It was conducted from 01.2017 to 12.2019 in centers of Russian Federation. The registry included patients over the age of 18 who were agreed to participate this study and had indications for CBA of AF. The study protocol did not provide for significant restrictions on inclusion criteria, procedure technique and postoperative follow-up. The data was collected prior to the CBA of AF, during hospitalization for CBA and on the 12-month follow-up.

Results. Participating centers enroll 980 patients according to inclusion criteria. CBA of AF was performed in 976 (99.6%) (mean age 59.7±9.2 years, 545 (55.8%) men) primary procedure - 840 (86.1%), re-ablation - 136 (13.9%). Paroxysmal AF occurred in 828 (84.8%) patients and persistent AF (mean time of persistence 4.4±3.7 months) - in 145 (15.1%) patients. The average procedure time was 108.1±33.3 minutes and mean fluoroscopy time was 24.9±13.6 min. Most of the procedures were performed under general anesthesia. Complications after AF CBA occurred in 53 (5.4%) patients. The most common complication was paresis of the phrenic nerve - 20 (37.7%) cases which were associated with lower temperatures of CBA application of the right pulmonary veins (τ=0.08; $p<0.05$). The features of antiarrhythmic and anticoagulant therapy were evaluated. A group of patients without adequate anticoagulant therapy in the postoperative period was identified. Due to COVID-19 restrictions only 374 (38.3%) patients completed 12-month follow-up. The recurrence of arrhythmia was occurred in 85 (22.7%) patients. Multivariate regression analysis revealed the following predictors of arrhythmia recurrence: the first procedure (OR 3.96; p=0.023), male sex (OR 1.77; p=0.014), duration of the procedure (min) (OR 1.01; p=0.007).

Conclusion. CBA is an effective and relatively safe procedure for the treatment of paroxysmal and persistent AF. Data from real clinical practice show a low proportion of serious complications of AF CBA. Data on the dynamics of drug therapy, including anticoagulant and antiarrhythmic therapy, were obtained. The attention of specialists performing AF catheter ablation and patient monitoring is required, since errors in patient management have been identified.

Keywords: atrial fibrillation; cryoballoon ablation; registry

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Corresponding author: Lev E. Korobchenko, E-mail: lev.korobchenko@gmail.com

L.E.Korobchenko - ORCID ID 0000-0001-7185-0983, T.A.Lyubimtseva - ORCID ID 000-0002-8651-7777, K.V.Davtyan - ORCID ID 0000-0003-3788-3997, A.G.Topchyan - ORCID ID 0000-0001-7605-6316, G.Yu.Simonyan ORCID ID 0000-0002-1118-5376, S.E.Serduk - ORCID ID 0000-0003-4479-6963, S.V.Korolev - ORCID ID 0000-0001-5513-2332, A.Ya.Kosonogov - ORCID ID 0000-0002-0961-3546, K.A.Kosonogov - ORCID ID 0000-0001-7482-4983, E.S.Tarasyuk - ORCID ID 0000-0002-8353-7510, K.A.Lubenkov - ORCID ID 0000-0002-6506-2646, A.S.Shulga - ORCID ID 0000-0003-0854-2990, E.A.Artyukhina - ORCID ID 0000-0001-7065-0250, A.Sh.Revishvili - ORCID ID 0000-0003-2855-303X, D.V.Kryzhanovskii - ORCID ID 0000-0002-5021-9129, R.E.Batalov - ORCID ID 0000-0003-1415-3932, S.Yu.Usenkov - ORCID ID 0000-0001-9553-9647, D.N.Khomutinin - ORCID ID 0000-0003-4006-9339, G.V.Kolunin - ORCID ID 0000-0002-9376-897X, V.E.Kharats - ORCID ID 0000-0002-6297-7859, A.A.Nechepurenko - ORCID ID 0000-0001-5722-9883, I.Sh.Sagitov - ORCID ID 0000-0002-5830-5056, N.I.Grachev - ORCID ID 0000-0001-6100-3625, N.L.Sharikov - ORCID ID 0000-0002-4517-1642, S.Yu.Chetverikov- ORCID ID 0000-0001-8377-202X, D.I.Perchatkin - ORCID ID 0000-0003-2865-7760, Yu.V.Virstyuk - ORCID ID - 0009-0006-7632-5620, F.G.Rzaev - ORCID ID 0000-0002-4094-7771, D.S.Lebedev- ORCID ID 0000-0002-2334-1663, E.N.Mikhaylov- ORCID ID 0000-0002-6553-9141

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Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice. The estimated prevalence of AF was 50 million people in the general population in 2020. Furthermore, the number of newly diagnosed cases continues to increase each year [1]. AF is associated with the development of adverse cardiovascular events, with the risks of stroke, myocardial infarction, and heart failure increasing by 2.4, 1.5, and 5 times, respectively [2, 3].

Currently, there is accumulating evidence regarding the positive impact of a sinus rhythm control strategy on the prognosis of patients with AF. This has strengthened the position of clinical guidelines on sinus rhythm control. Today, interventional catheter-based procedures have firmly established themselves in the armamentarium for treating patients with AF, with electrical isolation of the pulmonary veins (PVI) being the endpoint of catheter ablation [4, 5].

Cryoballoon Ablation (CBA) is one of the methods of PVI that has shown superiority over antiarrhythmic therapy (AAT) in the STOP-AF and CRYO-FIRST studies as a first-line treatment for AF. Furthermore, its efficacy and safety were found to be equivalent to radiofrequency (RF) ablation in several studies [6-9]. Technically, CBA uses a balloon catheter positioned at the PV orifice and cooled to negative temperatures by filling the internal balloon lumen with cryorefrigerant (nitric oxide). Cooling the myocardium to -40°C causes the intracellular formation of ice crystals, leading to cardiomyocyte damage and the subsequent development of reactive inflammation and replacement fibrosis, isolating the PV [10].

To study the efficacy and safety of CBA of AF in real clinical practice, the "Prospective Registry of Cryoablation for Atrial Fibrillation" was initiated in 2016, starting in January 2017. The registry is an observational, prospective, national, multicenter study conducted in medical institutions in the Russian Federation. The project is registered in the international clinical research system ClinicalTrials.gov, identification number NCT 03040037. The goal of the study was to investigate the clinical characteristics of patients referred for CBA, procedural parameters, and its efficacy in the early and long-term postoperative periods.

METHODS

Design

Patients were enrolled in the registry from January 2017 to December 2019. The inclusion criteria for the study were: (1) an indication for performing CBA of AF in patients aged over 18 years, (2) signed informed voluntary consent. Within the study, CBA of AF was performed both as a primary procedure and as a repeat procedure in patients with paroxysmal (PAF) and persistent (PeAF) forms of AF.

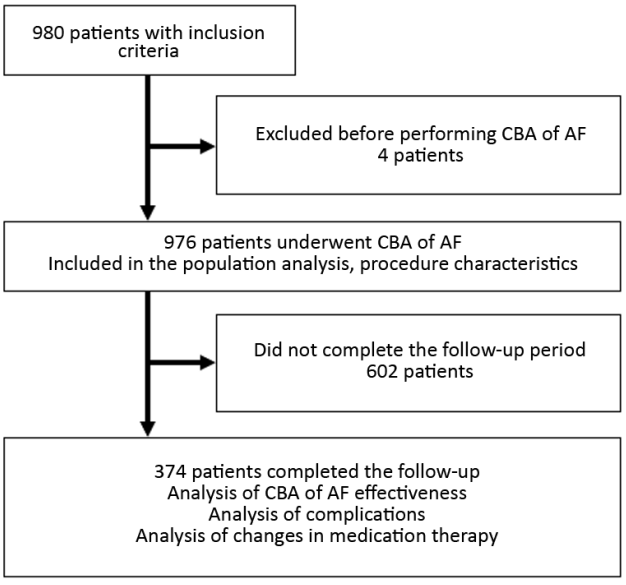

Fig. 1. Study diagram, where CBA is Cryoballoon Ablation, AF is Atrial Fibrillation.

Data collection and storage were carried out using the «Univers MDM» software (LLC «Univers Data,» St. Petersburg). The specifics of collecting clinical and demographic information were described previously [11]. All patients who participated in the study signed voluntary informed consent. Local ethical committees of each participating center approved the study protocol. The study was conducted in accordance with the Helsinki Declaration and the legislation of the Russian Federation.

Aim and endpoints

The aim of this registry was to study the characteristics of the CBA procedure of AF and the management of patients in real clinical practice in Russia. The primary endpoint was to describe the clinical and demographic characteristics of patients referred for CBA of AF.

Secondary endpoints included: (1) evaluation of the effectiveness and safety of the procedure in centers with different levels of experience in treating atrial fibrillation, (2) description of the technical aspects of performing the procedure, (3) acute and chronic complications of CBA, (4) identification of predictors of AF recurrence during the follow-up period.

Characteristics of the procedure

It should be noted that during data collection from the participating centers, preoperative preparation, anesthesia protocols, and the performance of CBA of AF were not strictly standardized. Patient management was carried out based on clinical guidelines and internal protocols of the participating institutions. The study included operators with varying levels of experience in interventional AF treatment (less than 100 procedures per year and more than 100 procedures per year) and CBA (less than 50 procedures per year and more than 50 procedures per year).

Table 1.

Clinical characteristics of patients participating in the study

	General population, n=976	Recurrent arrhythmias, n=134
Age, M±SD (min-max)	59.7±9.2 (27-80)	59.6±9.1 (29-72)
Women, n (%)	545 (55.8)	53 (39.6)
BMI <25 kg/m², n (%)	143 (14.7)	14 (10.4)
BMI 25-30 kg/m², n (%)	380 (38.9)	79 (59.0)
BMI ≥30 kg/m², n (%)	395 (40.5)	41 (30.6)
No BMI data	58 (5.9)	-
Paroxysmal AF, n (%)	828 (84.8)	116 (86.6)
Persistent AF, n (%)	145 (15.1)	15 (11.2)
No data on AF type, n (%)	3 (0.01)	3 (2.2)
Primary AF ablation, n (%)	840 (86.1)	124 (92.5)
Repeat AF ablation, n (%)	136 (13.9)	10 (7.5)
Hypertension, n (%)	744 (76.2)	101 (75.4)
Coronary artery disease, n (%)	183 (18.8)	28 (20.9)
Diabetes, n (%)	81 (8.3)	16 (11.9)
Stenting history, n (%)	59 (6.0)	7 (5.2)
CVA/TIA, n (%)	53 (5.4)	9 (6.7)
COPD, n (%)	44 (4.5)	7 (5.2)
Acute myocardial infarction, n (%)	34 (3.5)	5 (3.7)
Cardiomyopathy, n (%)	20 (2)	3 (2.2)
CHF I-II FC (NYHA), n (%)	188 (19.3)	25 (18.7)
CHF III-IV FC (NYHA), n (%)	4 (0.4)	-
LVEF ≤40%, n (%)	4 (0.4)	-
LVEF 41-49%, n (%)	28 (2.9)	4 (3.0)
LVEF ≥50%, n (%)	870 (89.1)	126 (94.0)
No data on LVEF, n (%)	74 (7.6)	4 (3.0)
LA ≤40 mm, n (%)	319 (32.3)	35 (26.1)
LA 41-50 mm, n (%)	403 (41.3)	69 (51.5)
LA >50 mm, n (%)	86 (8.8)	4 (3.0)
No data on LA size, n (%)	168 (17.2)	26 (19.4)

Note: BMI - body mass index; AF - atrial fibrillation; CVA - cerebrovascular accident; TIA - transient ischemic attack; COPD - chronic obstructive pulmonary disease; CHF - chronic heart failure; FC - functional class; LVEF - left ventricular ejection fraction; LA - left atrium.

Observation period

The observation period was 12 months, and the end of this period served as the main endpoint for postoperative follow-up. Patients underwent the follow-up either through in-person visits or using remote technologies. Recurrence of arrhythmia was defined as any supraventricular tachycardia lasting more than 30 seconds, detected through a 12-lead ECG, ECG monitor, telephone monitoring, or implanted loop recorders, identified after a 90-day blanking period. Due to restrictions related to the COVID-19 pandemic, a significant portion of patients could not complete the follow-up and was excluded from the assessment of long-term procedure efficacy, medication dynamics, and identification of arrhythmia recurrence predictors. However, the data from these patients were included in the characteristics of the overall population and CBA of AF procedure.

Statistical analysis

Descriptive statistics for variables are presented as the mean ± standard deviation, except for categorical variables, which are shown as percentages. To test for Gaussian distribution, the Kolmogorov-Smirnov test was used. For comparisons of variables with a Gaussian

distribution, the Student's t-test was applied; for variables with non-Gaussian distribution, the Wilcoxon test was used. Categorical variables were compared using the $\chi 2$ test. The Kendall test was applied to identify associations between variables. Logistic regression analysis was employed to identify predictors of arrhythmia recurrence. The analysis of arrhythmia recurrences was performed using the Kaplan-Meier method, and the standard error was calculated using Greenwood's formula. A p-value of <0.05 was considered statistically significant. Calculations were performed using RStudio software with the R programming language (©2023 Posit Software, PBC formerly RStudio, PBC).

RESULTS

A total of 33 medical institutions in the Russian Federation, where Cryoballoon Ablation of Atrial Fibrillation was technically possible in 2017, were invited to participate in the registry. 15 (46%) institutions participated in the registry. The registry included 980 patients, of whom 976 (99.6%) underwent CBA of AF, and 4 patients were excluded from the analysis. The 12-month follow-up point was completed by 374 (38.3%) patients. The study design is shown in Figure 1. The average number of patients included by each institution was 65.3±83.2 patients. The primary procedure of pulmonary vein isolation (PVI) was performed in 840 (86.1%) patients, and repeat AF ablation occurred in 136 (13.9%) cases.

The clinical characteristics of the patients are presented in Table 1. The study group included 545 (55.8%) women. PAF was present in 828 (84.8%) patients, and PeAF (mean duration 4.4±3.7 months) was present in 145 (15.1%) patients, with data missing for 3 (0.1%) patients. The majority of patients had obesity (395, 40.5%) and overweight (380, 38.9%). The most common comorbidity was arterial hypertension (AH), present in 744 (76.2%) patients. Most of the patients had a preserved left ventricular ejection fraction (LVEF), 870 (89.1%).

Characteristics of the procedure

The characteristics of the CBA of AF procedure are presented in Tables 2 and 3. The majority of CBA of AF procedures were performed by experienced operators: those with experience in AF ablation >100 procedures per year - 754 (77.3%) patients, and those with experience in CBA of AF >50 procedures per year - 804 (82.4%) patients. General anesthesia was used in 448 (45.9%) cases, and 185 (19.0%) procedures were performed under local anesthesia and sedation. Preoperative imaging (multi-slice computed tomography or magnetic resonance imaging) was conducted in 196 (20.1%) cases.

Most of the procedures, 778 (79.7%), were performed without the use of electroanatomical mapping systems. However, in 134 (14%) cases, transesophageal echocardiography was used for navigation, and in 479 (49%) cases, intracardiac echocardiography was utilized. Phrenic nerve function monitoring via stimulation mapping was performed in 889 (91.1%) patients, and esophageal temperature monitoring with a special sensor was done in 16 (1.6%) patients. The average procedure time was 108.1±33.3 minutes (Figure 2). However, no significant correlation was found between procedure duration and operator experience.

Left superior pulmonary vein (LSPV) ablation was performed in 955 (97.8%) patients, with one patient having previously undergone LSPV isolation. Intraoperative isolation was achieved in 952 (99.7%) patients, with 743 (77.8%) cases requiring one application, 178 (18.6%) requiring two, and 34 (3.6%) requiring three applications. The average temperature reached during LSPV ablation was -47.5±10.0°C.

Left inferior pulmonary vein (LIPV) ablation was performed in 947 (97.0%) patients, with 4 patients having previously undergone isolation of this vein and 8 patients not receiving treatment in this vein. One application was performed in 772 (81.4%) patients, two in 147 (15.6%), and three in 28 (3.0%) patients. Pulmonary vein isolation was successfully achieved in 933 (98.5%) patients. The

Table 2.

CBA of AF Characteristics

	GP, n=976
Procedure duration, min.	108.1±33.3
Fluoroscopy duration, min.	24.9±13.6
Application duration	
180 seconds, n (%)	332 (34.0)
240 seconds, n (%)	601 (61.6)
Individualized, n (%)	43 (4.4)
Anesthesia	
Sedation, n (%)	330 (33.1)
Local anesthesia, n (%)	185 (19.0)
General anesthesia, n (%)	448 (45.9)
No data, n (%)	13 (1.3)
Navigation	
Carto, n (%)	2
NavX, n (%)	3
Astrocard, n (%)	22 (2.3)
Other NS, n (%)	28 (2.9)
No NS used, n (%)	778 (79.7)
No data, n (%)	143 (14.7)

Note: GP - general population; NS - navigation system.

Table 3.

Pulmonary vein isolation, n (%)

	LSPV	LIPV	RSPV	RIPV
Total	955 (97.8)	947 (97.0)	951 (97.4)	941(96.4)
1 application	743 (77.8)	772 (81.4)	807(84.9)	791 (84.1)
2 applications	178 (18.6)	147 (15.6)	119 (12.5)	123 (13.1)
3 applications	34 (3.6)	28(3.0)	25 (2.6)	27 (2.8)
IOI	952 (99.7)	933 (98.5)	935(98.3)	917(97.4)

Note: LSLV, LILV, RSLV, and RILV - left and right, upper and lower pulmonary veins, respectively; IOI - intraoperative isolation..

average temperature during LIPV ablation was -44.8±9.3 °C. Right superior pulmonary vein (RSPV) ablation was performed in 951 (97.4%) patients and was successful in 935 (98.3%) cases. Additionally, 4 patients had previously undergone RSPV isolation, and 1 patient did not undergo treatment in this vein. One application was performed in 807 (84.9%) patients, two in 119 (12.5%), and three in 25 (2.6%). The average temperature during RSPV CBA was -48.4±9.5°C.

Right inferior pulmonary vein (RIPV) ablation was performed in 941 (96.4%) cases, with RIPV isolation achieved in 917 (97.4%) patients. Four patients had previously undergone RIPV isolation, and one patient did not undergo ablation. One, two, and three applications were performed in 791 (84.1%), 123 (13.1%), and 27 (2.8%) patients, respectively. The average temperature during RIPV CBA was -41.9±8.9°C.

In 8 cases, there was a common ostium of the left pulmonary veins, and in 2 cases, a single ostium of the right pulmonary veins.

The majority of procedures were performed using traditional CBA of AF protocols (application time 240 or 180 seconds), and only in 4% of cases were individualized protocols used with the «time-to-isolation» approach for pulmonary vein isolation. Additional radiofrequency (RF) energy to achieve pulmonary vein isolation was applied in 9 (0.9%) cases.

Complications

Complications after CBA of AF occurred in 53 (5.4%) patients (Table 4). The most common complication, observed in 20 (37.7%) cases, was transient phrenic nerve paresis, which was associated with lower temperatures during CBA of the right pulmonary veins (τ=0.08; p<0.05). No cases of persistent diaphragm paralysis were registered. Three patients died within 30 days after the procedure, but the cause of death was not specified.

Pneumothorax is an atypical complication of CBA of AF. However, based on the registry data, it was not possible to determine the exact cause of its development in one patient. The registry did not account for surgical access variations, and in this patient, it is possible that subclavian vein puncture was performed for the placement of a central venous catheter or additional electrodes.

Antiarrhythmic therapy

Preoperative AAT was administered to 880 (90.1%) patients (Table 5). The most commonly used drug group was beta-blockers, prescribed to 213 (21.8%) patients. Combined AAT, including a beta-blocker and a Class Ic or III drug, was used in 210 (21.5%) patients, while Class III drugs (sotalol – 189 (19.4%), amiodarone – 132 (13.5%)) were also frequently used. The least commonly used drug group was sodium channel blockers (Class Ic; at the time of registry enrollment, propafenone, lapacontine hydrobromide, and diethylamino propionyl ethoxycarbonylaminophenothiazine hydrochloride were available in Russia) – a total of 136 (13.9%) patients. Among the 321 patients who received Class III drugs, there were no contraindications for prescribing Class Ic in 153 patients.

In 96 (9.8%) patients, CBA of AF was chosen as first-line treatment (no AAT was administered prior to CBA of AF). The average age of this subgroup was 58.1±10.8 years. The majority of patients in this group had PAF – 67 (69.8%) compared to 6 (6.3%) with PeAF. The following comorbidities were reported in this subgroup: AH – 54 (56.3%); other comorbidities included a history of myocardial infarction in 2 patients, chronic heart failure (LVEF

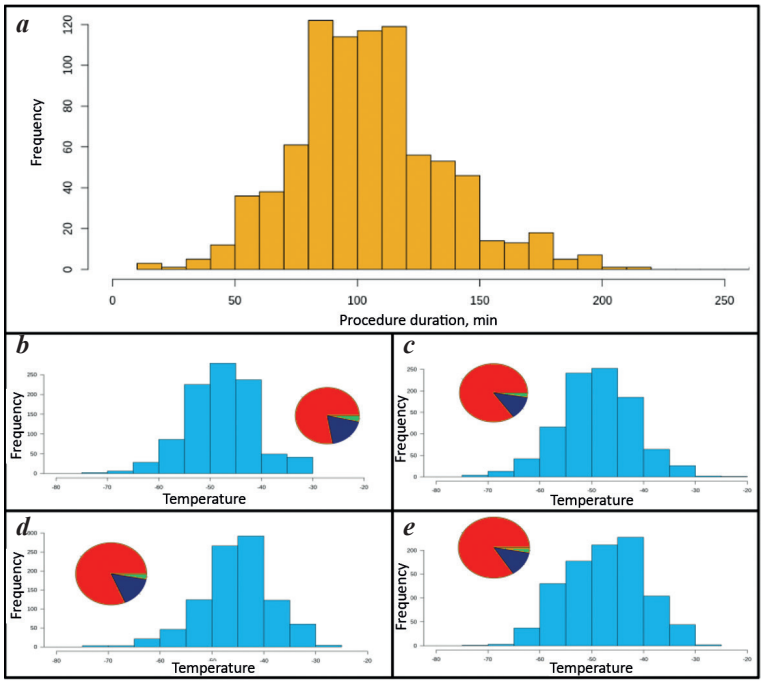

Fig. 2. Characteristics of pulmonary vein CBA: a - histogram of procedure time distribution; b-d - histograms of temperature distribution and pie charts of the number of applications (red - 1 application, blue - 2 applications, green - 3 applications) for CBA of LSLV, RSLV, LILV, and LILV, respectively.

Table 4.

CBA of AF complications

Transient phrenic nerve paresis, n (%)	20 (37.8)
Hematoma, n (%)	12 (22.6)
Hemopericardium, n (%)	5 (9.4)
Arteriovenous fistula, n (%)	3 (5.7)
Death within 30 days, n (%)	3 (5.7)
Femoral artery pseudoaneurysm, n (%)	2 (3.8)
Hemoptysis, n (%)	2 (3.8)
Atrial-esophageal fistula, n (%)	2 (3.8)
Pneumothorax, n (%)	1 (1.9)
Hemothorax, n (%)	1 (1.9)
Cardiac tamponade	1 (1.9)
Transient ischemic attack, n (%)	1 (1.9)
Total	53 (100)

- 54%) in 2 patients, and peripheral vascular diseases in 8 patients. The average left atrial diameter in this subgroup was 40.7±7.3 mm.

Anticoagulant therapy (ACT)

Before the CBA of AF, ACT was administered to 831 (85.1%) patients, while 145 (14.9%) patients did not receive ACT. Among the patients not receiving ACT, 41 (28.3%) were at high risk, 43 (29.7%) were at intermediate risk, and 61 (42.1%) were at low risk. In 399 (40.9%) cases, ablation was performed while continuing therapy with novel oral anticoagulants (NOACs), in 51 (5.2%) patients, therapy with warfarin was continued with target INR levels achieved, and in 330 (33.8%) cases, bridge therapy with low-molecular-weight heparin (LMWH) was used. In 196 (20.1%) cases, no data on the perioperative ACT regimen were available.

At the 12-month follow-up, 171 (45.7%) patients continued receiving ACT, while 203 (54.3%) patients had discontinued ACT. Among the patients who did not receive ACT, 201 (99%) were at intermediate or high risk of thromboembolic events (79 patients at high risk, 122 patients at intermediate risk).

Arrhythmia recurrences

The 12-month follow-up was completed by 374 (38.3%) patients. Among them, a documented recurrence of arrhythmia occurred in 85 (22.7%) patients (Fig. 3). Additionally, there were 16 early recorded episodes of arrhythmia that occurred during the blind period, which were not included in the evaluation of long-term effectiveness. No data on subsequent recurrences were available for this group of patients.

A trend towards more stable maintenance of sinus rhythm was observed in patients with PAF compared to PeAF: 78.1±2.3% (95% CI: 73.7-82.7%) vs 72.0±6.4% (95% CI: 60.6-85.6%), respectively. However, statistical significance was not reached, p=0.32. «Bonus applications» (additional CBA application after achieving PVI from the first application) were more common in the arrhythmia recurrence group (47.0% vs 40.5%), but no statistical significance was found (p=0.152).

The association with arrhythmia recurrence was examined for all parameters entered into the database. After constructing the correlation matrix of factors, pairs that correlated were excluded from the analysis. Univariate analysis revealed three factors with statistically significant correlations to arrhythmia recurrence: primary ablation, male sex, and procedure duration. Multivariate regression analysis showed that all three factors were independently associated with arrhythmia recurrence, though the odds ratio was minimal for procedure duration (Table 6).

DISCUSSION

The Prospective Registry of Cryoablation for Atrial Fibrillation is a national, prospective study on the effectiveness and safety of CBA for AF in real clinical practice. When characterizing the registry sample, it is notable that the majority of patients had no significant structural heart pathology, preserved LEVF, and minimal left atrial dilation, with a predominance of PAF (84.8%) and primary ablation procedures (86.1%), which aligns with similar studies [12, 13].

The low representation of PeAF in the registry is likely due to the perception of reduced effectiveness of CBA for AF in this form of arrhythmia, as CBA for AF was initially studied in patients with PAF [7-9] (and also approved by the FDA for the treatment of PAF [14]). However, it is also known that pulmonary vein isolation (PVI) has shown a positive impact on prognosis in patients with PeAF, leading to the STOP Persistent AF trial [15], which demonstrated the safety of using CBA for AF in PersAF with a sinus rhythm maintenance rate of around 55% over 12 months, which was further supported by registry studies [16]. The higher efficacy of sinus rhythm maintenance in the national registry is likely related to insufficient control and the small number of PeAF patients in the final observation group (15 patients). When deciding on interventional treatment for PeAF, it should be remembered that CBA for AF is an effective and safe method, comparable to radiofrequency ablation (RFA), and may be considered for this category of patients [17].

Interestingly, a small proportion of patients (96, 9.8%) underwent CBA as first-line therapy (i.e., without previous AAT). According to the Cryo AF Global Registry, the number of such patients in global practice approaches

Table 5.

Antiarrhythmic therapy

	At the time of inclusion (n=976)	Observation 12 months (n=374)
Lappaconitine hydrobromide, n (%)	47 (4.8)	7 (1.9)
Propafenone, n (%)	82 (8.4)	13 (3.5)
DAPEKA, n (%)	7 (0.7)	3 (0.8)
Beta-blockers, n (%)	213 (21.8)	139 (37.2)
Amiodarone, n (%)	132 (13.5)	16 (4.3)
Sotalol, n (%)	189 (19.4)	44 (11.7)
Combination AAT, n (%)	210 (21.5)	24 (6.4)
Without AAT, n (%)	96 (9.8)	128 (34.2)

Note: DAPEKA - diethylaminopropionylmethoxycarbonylaminophenothiazine; AAT - antiarrhythmic therapy

Table 6.

Anticoagulant therapy

	At the time of inclusion (n=976)	Observation 12 months (n=374)
Received ACT, n (%)	830 (85.0)	171 (45.7)
Apixaban, n (%)	143 (14.7)	34 (9.1)
Rivaroxaban, n (%)	406 (41.6)	75 (20.1)
Dabigatran etexilate, n (%)	150 (15.4)	30 (8.0)
Warfarin, n (%)	131 (13.4)	32 (8.6)
Did not receive ACT, n (%)	145 (14.9)	203 (54.3)

Note: ACT - anticoagulant therapy.

half of all CBA procedures for AF (42%) [13]. It is known that early rhythm control reduces the frequency of cardiovascular events, and early catheter ablation has higher efficacy, slowing disease progression [4, 18]. Early referral for catheter ablation can improve prognosis and quality of life for patients.

Nearly half (45.9%) of all procedures in the registry were performed under general anesthesia. Some studies have shown the advantage of performing the procedure under sedation due to reduced anesthetic time. However, there is currently no consensus regarding anesthetic management during catheter ablation for AF and the choice between general anesthesia and sedation. This largely depends on the experience and internal protocols of each specific institution, as reflected in the literature [6, 19].

Preoperative imaging (multislice computed tomography or magnetic resonance imaging) was performed in 196 (20.1%) patients. The vast majority of procedures were performed without using electroanatomical mapping systems, though transesophageal echocardiography or intracardiac echocardiography was used for additional imaging in over half of the cases.

Considering the study's limitations, the effectiveness of CBA for AF at 12 months was 78.1% for PAF and 72.0% for PeAF, which also aligns with the results of other registry studies. When analyzing these data, one should take into account the large number of patients lost to follow-up, the significant bias towards PAF, and specific treatment centers performing a high number of these procedures [12, 13].

According to the registry, operators most commonly use one application for PVI lasting 240 seconds, though the «bonus application» strategy (additional CBA application after achieving PVI from the first application) is used in 15-20% of cases. The dosing of cryoapplications is also nuanced. Technically, CBA for AF is considered a single-shot procedure, where one application should be sufficient for PVI. However, in clinical practice, a «bonus application» strategy is sometimes used after PVI is achieved. This strategy was introduced in foundational studies with first-generation cryoballoons. However, with the advent of second-generation cryoballoons, studies have emerged focusing on reducing the dose of cryoapplication. It is now known that routine use of the «bonus» strategy does not lead to better ablation outcomes. Subsequent comparisons of different cryoapplication durations (180 and 240 seconds) also showed no difference in PVI and sinus rhythm maintenance. The most relevant strategy today is the individualized approach, selecting the application time based on the «time to isolation» parameter. Individualized approaches reduce the duration of the procedure without affecting its effectiveness, but according to the registry, individualized approaches were relatively rare, requiring attention from operators [20-24].

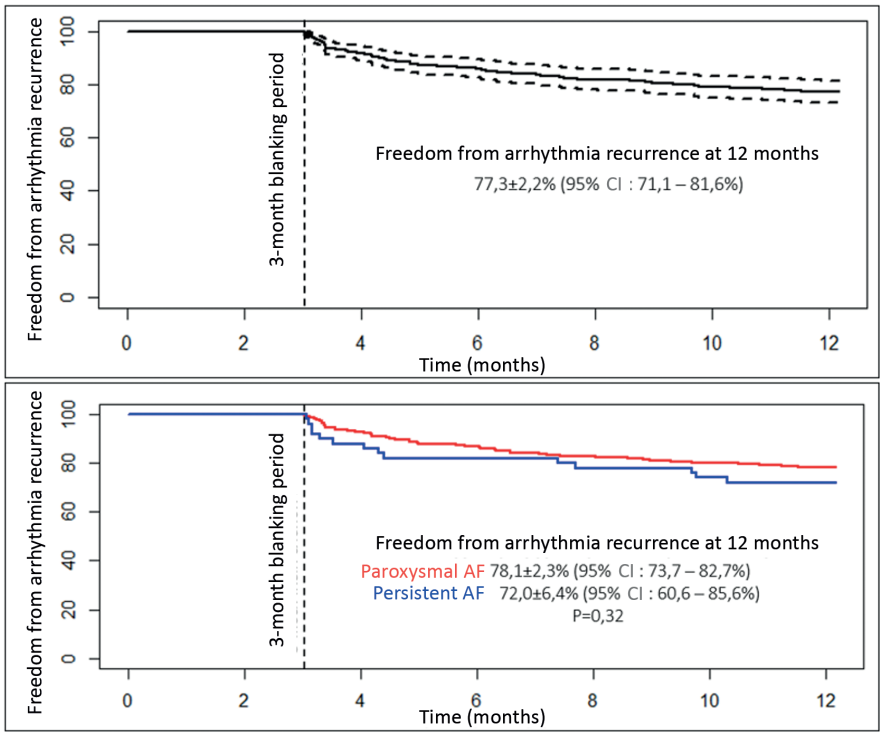

Fig. 3. Sinus rhythm maintenance curves.

The low complication rate for CBA for AF speaks to its safety. The most common complication, as expected, was transient phrenic nerve palsy, which was associated with lower temperatures during the ablation of the right pulmonary veins.

Regarding AAT, the registry data show a traditional predominance of beta-blockers and class III antiarrhythmic drugs [25]. Beta-blockers were the most common AADs in the patients included in the registry. Specific indications for beta-blocker use (antihypertensive, antianginal, chronic heart failure therapy) cannot be determined within the scope of the study. However, it should be remembered that, for AF therapy, beta-blockers are not intended for long-term sinus rhythm control (exception: when

Table 7.

Predictors of arrhythmia recurrence

Factor	OR	CI	P
Univariate analysis			
First procedure	2.2	1.18-4.58	0.021
Male gender	1.25	0.86-1.82	0.242
Procedure duration, min	1.01	1.00-1.01	0.016
Multivariate analysis			
First procedure			
Male gender	1.62	1.04-2.55	0.036
Procedure duration, min	1.01	1.00-1.01	0.008

combined with Ic-class drugs for the prevention of complications). Furthermore, despite the lack of data on prior AAT, considering the overall population characteristics, there was insufficient prescription of Ic-class drugs, with a preference for class III AADs. While amiodarone is clearly indicated as a medication for structural heart disease or as a last-line therapy in various clinical guidelines, the approach to sotalol differs significantly between national and international guidelines. In national guidelines, sotalol may be used for preventing AF recurrences in patients without severe organic heart disease, without impaired pumping function, and without CHF (Class IIA, Level 2b), while ESC and AHA/ACC guidelines classify sotalol under Class IIb and Level 2b, respectively. The likely reason for this difference is the study by L. Valembois et al., which showed an increased risk of death from all causes when using sotalol compared to the placebo group (OR=2.23; 95% CI: 1.03-4.81). Additionally, it is known that sotalol significantly affects the QT interval, and there is evidence of individual «hypersensitivity» to sotalol due to reduced repolarization reserve. Given this, experts from AHA/ACC recommend initiation and titration of sotalol therapy only in hospital settings [26-31].

A separate discussion is warranted regarding ACT. Unfortunately, there remains a category of patients who did not receive ACT in the preoperative and postoperative periods, despite formal indications based on the CHA_2DS_2-VASc score. It is known that catheter ablation of AF (including «effective» ablation) is not a reason to discontinue ACT, and in the initial postoperative period (the first 2 months), ACT is actually indicated, even for patients at low thromboembolic risk. Subsequently, the decision to discontinue ACT is made based on CHA_2DS_2-VASc scores and data on arrhythmia recurrence [26, 27].

Additionally, the registry data demonstrate that the issue of perioperative ACT remains unresolved. It is important to note that catheter ablation of AF is a procedure with a high risk of bleeding and increased risk of thromboembolic complications. According to the registry, about one-third of all patients were managed with a bridging therapy regimen, which contradicts current guidelines for the diagnosis and treatment of AF [26]. Currently, the most relevant perioperative ACT regimens are: continuous therapy and temporary interruption. Meta-analyses of large studies have shown a reduction in major bleeding rates with continuous NOAC therapy compared to vitamin K antagonists [33, 34]. Continuous vitamin K antagonist therapy, compared to bridging therapy, also showed no difference in the rate of major bleeding [35]. Limitations to the use of continuous therapy may include the official instructions for NOACs. Current clinical guidelines, approved by the Ministry of Health of Russia's expert council, allow for continued oral anticoagulation during the perioperative period and a short interruption of NOACs before ablation.

Compared to the results of the first survey of specialists on CBA [17], the average procedure time and the number of cryoapplications have significantly decreased, as well as the need for additional radiofrequency catheter applications to complete the isolation of pulmonary veins. This is explained by the use of second-generation balloons and increasing operator experience. There is also an increase in CBA efficiency; however, direct comparison of this indicator is difficult, as the 2015 survey considered arrhythmia recurrences during the first 6 months, while the registry shows a low percentage of patients remaining under observation. Additionally, there is a noted increase in the proportion of procedures performed under the control of electroanatomical mapping.

Study limitations

A significant limitation of the study is the lack of 12-month follow-up data for two-thirds of patients, which could have influenced the results of the assessment of predictors for arrhythmia recurrence. As a result of this limitation, there may also be an underestimation of delayed complications from ablation and adverse clinical events. The registry did not provide for the standardization of ablation procedures and arrhythmia recurrence registration, but this allowed for an analysis of real-world clinical data. Another limitation of the study is its conduct during the COVID-19 pandemic, which impacted the quality of postoperative data collection and potentially affected the ablation outcomes in patients who had contracted the infection.

CONCLUSION

Cryoballoon ablation is an effective and relatively safe procedure for the treatment of paroxysmal and persistent atrial fibrillation. Data from real clinical practice reflect a low proportion of serious complications from the procedure. For the first time, data have been obtained on the dynamics of medication therapy, including anticoagulant and antiarrhythmic treatment. Attention is needed from specialists performing AF catheter ablations and monitoring patients, as deviations in patient management from the approaches outlined in clinical guidelines have been identified.

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