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EFFICACY OF DIFFERENT CRYOBALLOON ABLATION STRATEGIES IN PATIENTS WITH PERSISTENT ATRIAL FIBRILLATION

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Aim. To study the effectiveness of "extended" cryoballon ablation in patients with a persistent form of atrial fibrillation (AF) and to determine the risk factors for AF recurrence after cryoablation.

Methods. The study included 89 patients (62±10 years, 24 [27%] men) with a persistent form of AF. The patients were randomized into two groups: in the 1st, the pulmonary veins (PV) cryoablation was performed (n=48 [53.9%]); in the 2nd, the PV cryoablation was performed in combination with cryoablation of the posterior wall of the left atrium (n=41 [46.1%]). The number of patients at high risk of thromboembolic events predominated in Group 2 (p=0,03). There is a high frequency of taking antiarrhythmic drugs of class III in this group (p=0.018). The follow-up period was 12 months. Clinical efficacy was assessed during a survey and daily ECG monitoring at face-to-face visits after 3, 6 and 12 months.

Results. Antral isolation of PV was achieved in all 89 (100%) patients in both groups. In group 2, the average number of applications in the posterior wall of the PV was 10 [9; 13]. The effectiveness of cryoablation in group 1 by the end of the 12-month follow-up period was 54.2%, in group 2 - 56.1%. The complication rate (6.7%) in both groups did not differ statistically (p=0.683). The risk of arrhythmia recurrence didn't depend on the strategy of cryoablation in postablation period (p=0.834). When conducting a single-factor analysis, a statistically significant effect on the probability of AF recurrence in the period of 3-12 months in group 1 was caused by AF recurrence in the blind period (95% confidence interval (CI): 1.5-27.7, p=0.013), in group 2 belonging to the female sex (95% CI: 1.2-24.6, p=0.032) and AF relapse in the blind period (95% CI: 1.5-128.5, p=0.020). During multivariate analysis in group 2, a statistically significant influence on the risk of AF recurrence in the period of 3-12 months was exerted by belonging to the female sex (hazard ratio (HR) 7.84; 95% CI 1478-42,23; p=0.016) and the presence of early AF recurrence (HR 20.36; 95% CI 1.99-208.23; p=0.011).

Conclusion. Extended cryoablation in terms of efficiency and safety was comparable with the standard cryoablation. Early recurrence of AF (in the first 3 months after the intervention) turned out to be an independent risk factor for AF recurrence in the long-term period up to 12 months after cryoablation in both groups.

Key words: atrial fibrillation; cryoballon ablation; pulmonary veins; extended cryoaballon ablation; left atrium

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Catheter ablation (isolation) of pulmonary veins (PV) for persistent atrial fibrillation (AF) has a high level of recommendation in cases of symptomatic course of persistent AF, decreased quality of life, ineffectiveness of antiarrhythmic therapy and development of heart failure [1]. It is known that the efficacy of catheter ablation limited only to the PV area in persistent AF is significantly inferior to the same intervention in patients with paroxysmal form of this arrhythmia [2]. It has been shown that the evolution of AF from paroxysmal to persistent form may reflect the progression of electrical and structural remodeling of atrial myocardium as elements of atrial cardiomyopathy [3, 4]. These processes may contribute to the formation of an «arrhythmogenic» source of AF outside the PV. It is assumed that the emergence of technologies for verification of the triggering factors of AF lying outside the PV will improve

the effectiveness of endocardial interventions in persistent AF. Recently, there have been data on the prospects of using «extended» cryoballon ablation (CBA), which involves additional cryo-interventions in the region of the posterior wall of the left atrium (LA) in addition to isolation of the PV antral part [5].

The concept of extended cryoablation in LA assumes that the triggers of AF can be eliminated without their precise electro-anatomic identification. Therefore, the aim of our study was to comparatively investigate the efficacy of PV CBA and extended LA CBA in patients with persistent AF.

METHODS

The prospective randomized study included patients with persistent AF who had indications for CBA according to current international and national guidelines. Patients were randomized into two groups using the closed envelope method. The first group included patients who were randomized to undergo endocardial PV CBA. The second group included patients who were supposed to undergo extended CBA of the LA, which involved PV antral isolation combined with cryoablation of the posterior wall of the LA (Fig. 1). Unequal randomization across the groups of included patients was due to their refusal of further follow-up and desire to withdraw from the study.

All patients underwent general clinical examination before the intervention: general and biochemical blood tests, control of thyroid hormones, 12 channel electrocardiogram (ECG), Holter ECG monitoring, transthoracic echocardiography, multispiral computed tomography of the heart with contrast to assess LA volume and PV anatomy. CBA was performed under endotracheal anesthesia. Intraoperatively, transesophageal echocardiography was performed to exclude atrial thrombosis, the effect of spontaneous echo contrast, and to control access to the left atrium during atrial septal puncture.

Antral PV isolation in both groups was performed according to the technique described previously [6]. The FlexCath Advance steerable intracardiac intra-arterial introdescer (Medtronic, Minneapolis, MN, USA) and the Arctic Front Advance 28 mm balloon catheter (Medtronic, Minneapolis, MN, USA) were inserted into the LA cavity via a guide catheter. PV mapping was performed using an Achieve Advance 20 mm circular diagnostic catheter (Medtronic, Minneapolis, MN, USA). Under fluoroscopic control, a multipolar guided diagnostic catheter (EP-XT, Boston Scientific, MN, USA) was placed in the coronary sinus area. Cryoablation was performed under the control of activated coagulation time of at least 350 seconds. In the antral part of each PV, ablation with a cryoballoon was performed once with a duration of exposure of 240 seconds each and reaching a temperature of -40 to -60 °C. The criterion of PV isolation was the presence of blockade of the input and output of electrical impulses 20 minutes after the completion of cryoablation. In case of absence of persistent PV isolation, repeated 180-second exposure was performed. During cryoablation of the right PV, high-amplitude stimulation of the right diaphragmatic nerve (10-25 mA; 1000-1200 ms) was performed using a diagnostic electrophysiologic catheter located in the superior vena cava. Exposure was terminated when there were signs of diaphragmatic nerve paresis (weakening or cessation of diaphragm movement in response to stimulation).

In group 2, in addition to PV CBA, a series of cryoballoon applications were performed in the region of the posterior wall of the LA. CBA of the posterior wall of the LA was performed according to the technique previously described by A.Aryana et al (2018) [5]. Isolation of the posterior LA wall was performed segmentally, with fixation of the circular catheter alternately in each PV (Fig. 1). From 9 to 13 cryoapplications were performed in the region of the posterior wall of the LA, with the duration of each exposure from 120 to 180 seconds. Intraoperatively, the effectiveness of LA posterior wall isolation using navigation mapping was not assessed. CBA in the region of the posterior wall of the LA was performed under control of the temperature sensor in the esophagus. When the temperature in the esophagus decreased below +15 °C, the exposure was stopped.

All patients were followed up for 1 year postoperatively. The criterion of efficacy was the absence of sustained (lasting more than 30 seconds) tachyarrhythmias (AF, atrial flutter, atrial tachycardia) registered according to ECG and ECG Holter monitoring, occurring after the end of the three-month «blanking» period, or subjective sensations of episodes of palpitations during the follow-up period. Early recurrences were episodes of AF recorded in the first 3 months after CBA. Holter ECG monitoring with heart rate assessment was performed on the 1st day after surgery, at 3, 6, and 12 months. After CBA, antiarrhythmic therapy with class IC or III drugs

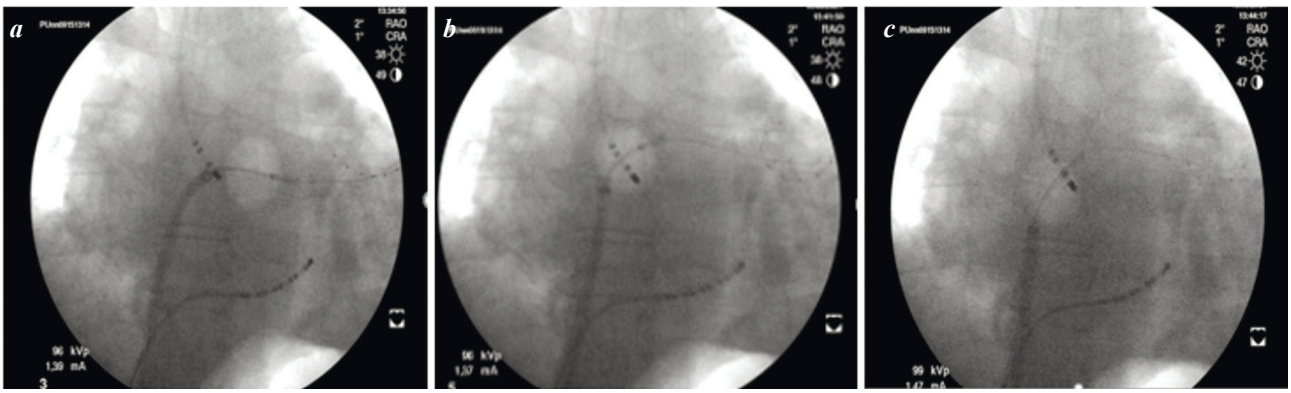

Fig. 1. Different cryoballoon positioning (a, b, c) during posterior left atrial wall cryoablation where the temperature sensor-electrode is placed in the esophagus.

(except amiodarone) or beta-blockers was resumed for up to three months (« blanking period») with further withdrawal. Anticoagulant therapy was resumed no later than 3 hours after completion of ablation. The period of anticoagulant therapy prescription was at least two months, with direct oral anticoagulants being preferred. At the end of this period, the decision to continue continuous anticoagulant therapy was based on the CHA_2DS_2-VASc thromboembolic risk score. Before the intervention and 12 months after the intervention, patients with recurrent

Table 1.

Clinical and anamnestic characteristics of patients

Indicator	PV CBA (n=48)	PV CBA and LA posterior wall (n=41)	P	V	OR; 95% CI
Age, Me [IQR], years	62.0 [57.5; 67.5]	60.0 [54.0; 67.0]	0.249	-	-
Sex female, n (%)	35 (72.9%)	30 (73.2%)	0.979	0.003	1.0; 0.4-2.5
Sex male, n (%)	13 (27.1%)	11 (26.8%)			
BMI, M±SD (95% CI), kg/m^2	30.8±4.9 (29.4-32.3)	30.0±4.3 (28.6-31.3)	0.373	-	-
CHA_2DS_2-VASc, n (%), points					
0	7 (14.6%)	1 (2.4%)	0.03	-	-
1	7 (14.6%)	16 (39.0%)	0.06	-	-
≥2	34 (70.8%)	24 (58.5%)	0.2	-	-
Arterial hypertension, n (%)	34 (70.8%)	35 (85.4%)	0.129	0.174	2.4; 0.8-7.0
Diabetes mellitus, n (%)	7 (14.6%)	5 (12.2%)	1.0	0.035	0.8; 0.2-2.8
Stroke/TIA, n (%)	3 (6.3%)	3 (7.3%)	1.0	0.021	1.2; 0.2-6.2
CHF, n (%)	7 (14.6%)	8 (19.5%)	0.580	0.066	1.4; 0.5-4.3
Coronary heart disease, n (%)	12 (25.0%)	7 (17.%)	0.441	0.096	0.6; 0.2-1.8
Myocardial infarction, n (%)	3 (6.3%)	4 (9.8%)	0.699	0.065	1.6; 0.3-7.7
TBA, n (%)	10 (20.8%)	4 (9.8%)	0.243	0.152	0.4; 0.1-1.4
Coronary bypass surgery, n (%)	1 (2.1%)	1 (2.4%)	1.0	0.012	1.2; 0.1-19.4
Chronic kidney disease, n (%)	1 (2.1%)	2 (4.9%)	0.593	0.077	2.4; 0.2-27.6
Maximum duration of the episode, n (%), months					
0-3	15 (31.3%)	9 (22.0%)	0.148	-	-
3-6	13 (27.1%)	21 (51.2%)	0.8	-	-
6-12	19 (39.6%)	10 (24.4%)	0.2	-	-
More than 12	1 (2.1%)	1 (2.4%)	0.3	-	-
History of atrial fibrillation, n (%), years					
<1	3 (6.3%)	1 (2.4%)	0.59	-	-
1-2	9 (18.8%)	8 (19.5%)	0.76	-	-
>2	36 (75.0%)	32 (78.0%)	0.5	-	-
History of RFA CI, n (%)	1 (2.1%)	4 (9.8%)	0.176	0.166	5.1; 0.5-47.4
Antiarrhythmic therapy					
AAD class Ic, n (%)	20 (41.7%)	21 (51.2%)	0.367	0.096	1.5; 0.6-3.4
BB before intervention, n (%)	42 (87.5%)	35 (85.4%)	1.0	0.031	0.8; 0.2-2.8
AAD class III, n (%)	22 (45.8%)	29 (70.7%)	0.018	0.251	2.9; 1.2-6.9
AAD class IV, n (%)	0	2 (4.9%)	0.209	0.164	-
Digoxin, n (%)	2 (4.2%)	4 (9.8%)	0.408	0.111	2.5; 0.4-14.3
LVEF, Me[IQR], %	60.0 [55.0-60.0]	55.0 [50.0-60.0]	0.446	-	-
LA APD, Me[IQR], cm	4.4 [4.0-4.6]	4.3 [4.1-4.6]	0.849	-	-
EchoCG LA volume, M±SD (95% CI), ml	80.4±16.7 (75.6-85.3)	81.0±15.4 (76.0-85.8)	0.877	-	-
LA CT volume, M±SD (95% CI), ml	89.7±28.8 (80.6-98.8)	96.9±8.4 (87.8-105.9)	0.263	-	-

Note: hereinafter CBA - balloon cryoablation; PV - pulmonary veins; LA - left atrium; OR - odds ratio; CI - confidence interval; BMI - body mass index; TIA - transient ischemic attack; CHF - chronic heart failure; TBA - transluminal balloon angioplasty; RFA CI - radiofrequency ablation of cavotricuspidal isthmus; AAD - antiarrhythmic drugs; BB - beta-blockers; LVEF - left ventricular ejection fraction; APD - anteroposterior dimension; EchoCG - transthoracic echocardiography; MSCT - multispiral computed tomography.

AF/atrial flutter (AFt) were assessed for quality of life using the SF-36 questionnaire and evaluated for the severity of AF symptoms using the EHRA scale.

Statistical analysis

The SPSS Statistics software package version 26.0 (SPSS, Chicago, IL, USA) was used for statistical analysis of the obtained data. The normality of the distribution was checked using the Shapiro-Wilk criterion. The Mann-Whitney test was used to analyze quantitative data with a distribution other than normal in 2 independent samples; the Student's t-test was used to evaluate quantitative data with a normal distribution (if there was a statistically significant difference in variance, the Student's t-test modified by Welch was used). Pearson's chi-square or Fisher's exact test was applied to assess qualitative features in the 2 groups of patients, depending on the minimum expected number. For traits with statistically significant differences, odds estimate with 95% confidence interval (CI) were performed, and a measure of association between nominal traits was determined. Multifield contingency tables followed by post-hoc analysis were used to analyze nominal traits in the 3 groups. The McNemar test was used to assess nominal traits in linked populations at 2 stages of follow-up. A prognostic model was developed by binary logistic regression method to determine the risk of AF recurrence. Kaplan-Meier curves were constructed to graphically reflect the impact of various factors on CBA efficiency. Single- and multivariate analyses using Cox regression were performed to identify independent risk factors for recurrent AF after CBA. Only significant indicators were included in the multivariate analysis. Differences were considered statistically significant at $p<0.05$.

RESULTS

A total of 89 patients with persistent form of AF were included in the study. 48 (53.9%) patients were randomized to group No.1, 41 (46.1%) patients were randomized to group No.2. According to the randomization conditions, all patients in group 1 underwent PV CBA, and patients in group 2 underwent PV CBA + posterior wall of the LA. Table 1 summarizes the comparative clinical and anamnestic characteristics of patients in both groups. The mean age of the patients was 62±10 years. Women 65 [73%] were predominant among those included in the study. The mean duration of history of AF was 3.0 [1.0; 6.0] years, and the mean duration of maximum AF episode was 5.15 months (95% CI: 4,20-6,10). The mean LA volume was 80.6±16.05 (95% CI: 77.28-84.05) mL. Computed tomography revealed a common PV vestibule in 30 (33.7%) patients. Statistically significant differences between both groups of patients were found when assessing the risk of thromboembolic complications using the CHA_2DS_2-VASc scale, as well as the frequency of taking class III antiarrhythmic drugs. Depending on the number of CHA_2DS_2-VASc scores, all patients were divided into 3 groups: group 1 included patients with 0 points, group 2 included patients with 1 point, and group 3 included patients with 2 points or more. When comparing patients in each group with different risk of thromboembolic complications, statistically significant differences were obtained with CHA_2DS_2-VASc scores of 0. Thus, when comparing the patients, 0 points were predominantly observed in the PV CBA group, which indicates that the patients who underwent PV CBA and LA posterior wall CBA had a higher risk of thromboembolic complications (p=0.03). Also, a higher frequency of class III antiarrhythmic drugs was found among these patients (n=29 [70.7%]). According to the other signs obtained because of clinical-instrumental examination and anamnesis collection, no statistically significant differences were found between patients of both groups.

Intraoperative parameters (Table 2) were not statistically significantly different between the groups. All patients underwent electrical and/or drug-induced cardioversion before the intervention. 43 (48.3%) of 89 patients underwent intervention against the background of sinus rhythm. The remaining 46 (51.7%) out of 89 patients subsequent-

Table 2.

Intraoperative rates, complication rates and arrhythmia recurrence in the two treatment groups

	PV CBA (n=48)	PV CBA and LA AW (n=41)	P	V	OR; 95% CI
LV isolation, n (%)	48 (100%)	41 (100%)	-	-	-
Duration of operation, Me[IQR], min	180 [80; 240]	200 [160; 330]	0.71	-	-
Radiation dose, Me[IQR], mSv	2.1 [1.8; 3.5]	2 [1.6; 3]	0.52	-	-
Fluoroscopy time, Me[IQR], min	7 [5; 11]	7.2 [5.5; 12]	0.92	-	-
Number of impacts by ZS, Me[IQR], n	-	10.0 [10.0; 11.0]	-	-	-
Thrombosis at the puncture site, n (%)	4 (8.3%)	2 (4.9%)	0.683	0.069	0.6; 0.1-3.3
RFA CI, n (%)	6 (12.5%)	7 (17.1%)	0.563	0.065	1.4; 0.4-4.7
Total LV vestibule, n (%)	15 (31.3%)	15 (36.6%)	0.596	0.056	1.3; 0.5-3.1
Early recurrences of AF/AFt in the blanking period, n (%)	15 (31.3%)	12 (29.3%)	0.839	0.021	0.91; 0.37-2.26
Long-term recurrences of AF/AFt (3-12 months), n (%)	22 (45.8%)	18 (43.9%)	0.855	0.019	0.93; 0.4-2.14
AFt, n (%)	3 (3.35%)	3 (3.35%)	1.0	0.021	1.18; 0.23-6.21
Paroxysmal AF after CBA, n (%)	8 (9%)	10 (11.2%)	1.0	0.017	1.09; 0.41-2.89
Persistent AF after CBA, n (%)	9 (10.1%)	7 (7.9%)	0.79	0.048	0.78; 0.27-2.28

Note: Hereinafter, hereinafter RW stands for rear wall; AF - atrial fibrillation; AFt - atrial flutter.

ly developed a recurrence of AF and the intervention was performed against the background of arrhythmia recurrence. In 9 patients, restoration of sinus rhythm was noted during PV isolation, and 37 patients underwent electrical cardioversion intraoperatively after CBA. Antral electrical isolation of the PV was achieved in all 89 (100%) patients. The duration of surgery in both groups averaged 180 [157.5;240] min, fluoroscopy time 7.11 [5.41;11.7] min. In group 2, the mean number of applications in the posterior wall region of the LA was 10.0 [9.0; 13.0]. In 7 (7.8%) patients, a decrease in esophageal temperature below 20 °C was noted during CBA, and cryo-intervention was interrupted. In 7 (7.8%) patients there was a decrease in esophageal temperature during one of the exposures in the region of the posterior wall of the LA to +16-17 °C and was observed predominantly at 130-140 sec. Therefore, further cryablation was discontinued. Esophageal temperature recovered over 20°C within 1 minute. Radiofrequency ablation of the cavotricuspid isthmus due to concomitant typical atrial flutter was performed in 6 (12.5%) and 7 (17.1%) patients, respectively. The incidence of the only reported complication (venous thrombosis at the puncture site) was reported in 6 (6.7%) patients; the results in both groups were not statistically significantly different (p=0.683). No major complications (death, cardiac tamponade/hemopericardium, major bleeding, atrial-esophageal fistula, diaphragmatic nerve paresis) were reported during the follow-up period. The effectiveness of the intervention depending on the two CBA strategies, assessed using the log-rank (Mantel-Cox) criterion, was statistically insignificant (p=0.834) (Fig. 2). The mean time to recurrence of AF or atrial flutter (AFt) for patients who underwent PV CBA was 246.35±20.98 days (95% CI: 205.23-287.48), and for patients who underwent PV CBA and LA posterior wall CBA was 253.46±22.66 days (95% CI: 209.05-297.88).

CBA efficacy by the end of the 12-month follow-up period (excluding the blanking period of the first 3 months after CBA) was 54.2% in group 1 and 56.1% in group 2 (Fig. 2). Kaplan-Meier analysis showed that the mean time to occurrence of AF/AFt recurrence after performing CBA, regardless of intervention volume, was 249.63±15.4 days (95% CI: 219.44-279.82).

The study evaluated risk factors for recurrent AF/AFt (Table 3). In the present study, traditional risk factors such as total PV vestibule, LA volume, and duration of history of AF had no statistically significant effect on the risk of recurrent AF/AFt. In single-factor analysis, only recurrence of AF/AFt in the blanking period had a statistically significant effect (p=0.013) on the probability of recurrence of AF/AFt in group 1, which increased the probability of late arrhythmia recurrence 6.4-fold (95% CI: 1.5-27.7). For patients in group 2, in the single-factor analysis, a statistically significant influence on the probability of late recurrence of AF

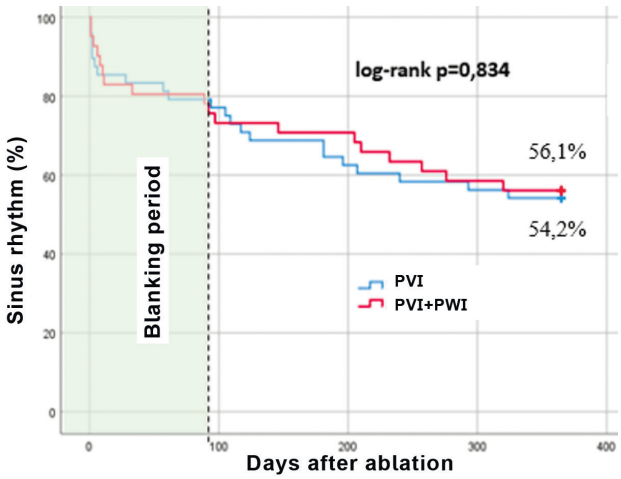

Fig. 2. Frequency of preservation of sinus rhythm in groups of patients.

Table 3.

Single- and multivariate analysis of risk factors for atrial fibrillation recurrence after cryoballoon ablation

	PV CBA		PV CBA and LA AW	
	HR (95% CI)	p	HR (95% CI)	p
Age, years	1,0 (0,9-1,1)	0,710	1,0 (0,98-1,12)	0,218
Gender, female	2,4 (0,7-8,9)	0,189	5,3 (1,2-24,6)*	0,032
BMI	1,1 (0,97-1,26)	0,126	0,95 (0,82-1,10)	0,499
CHA_2DS_2-VASc	0,94 (0,44-2,04)	0,882	1,4 (0,4-4,3)	0,602
Arterial hypertension	1,2 (0,34-4,16)	0,791	0,75 (0,13-4,3)	0,745
Diabetes mellitus	3,6 (0,61-20,38)	0,159	2,1 (0,3-14,2)	0,446
Stroke / TIA	2,5 (0,21-29,6)	0,467	-	0,999
CHD	1,7 (0,34-8,6)	0,519	0,4 (0,1-2,0)	0,242
Ischemic heart disease	0,3 (0,1-1,3)	0,105	0,95 (0,2-4,9)	0,951
Myocardial infarction	0,6 (0,04-6,8)	0,657	4,4 (0,4-46,4)	0,218
AF MED	1,1 (0,4-3,2)	0,840	0,6 (0,2-2,2)	0,435
History of AF	1,2 (0,5-3,4)	0,665	1,2 (0,3-4,3)	0,8
LVEF	1,0 (0,9-1,0)	0,251	1,1 (0,96-1,15)	0,270
LA APD	2,9 (0,7-12,6)	0,161	0,31 (0,05-1,8)	0,195
LA volume Echocardiogram	1,0 (0,97-1,05)	0,521	0,97 (0,9-1,0)	0,200
Volume of LA CT	1,0 (1,0 -1,05)	0,053	1,0 (0,99-1,0)	0,540
Restore HR@	1,2 (0,4-3,9)	0,715	0,8 (0,2-2,8)	0,732
Recurrence of AF and AFt&	6,4 (1,5-27,7)	0,013	14,0 (1,5-128,5)#	0,20
Total LV vestibule	1,1 (0,3-3,6)	0,938	1,8 (0,5-6,6)	0,358
PV insulation	1,3 (0,3-4,7)	0,738	0,5 (0,2-2,0)	0,358

Note: HR - hazard ratio; MED - maximum episode duration; @ - during the intervention; & - during the blanking period; * - OR 7.87 (1.47-42.23), p=0.016; # - OR 20.36 (1.99-208.23), p=0.011.

was female sex, and, as in group 1, recurrence of AF/AFt in the first 3 months.

In multivariate analysis, the same factors had a statistically significant effect on the risk of recurrent AF. Considering the identified factors of AF recurrence, a prognostic model was developed to determine the risk of AAF recurrence in the postablation period by binary logistic regression. The regression model obtained is statistically significant (p=0.001). Based on the values of regression coefficients, paroxysm of AF/AFt in the blanking period and female gender have a direct association with the probability of late recurrence of AF and increases the probability of arrhythmia recurrence during the follow-up period by 20.36-fold (95% CI: 1.99-208.23) and 7.87-fold (95% CI: 1.47-42.23), respectively.

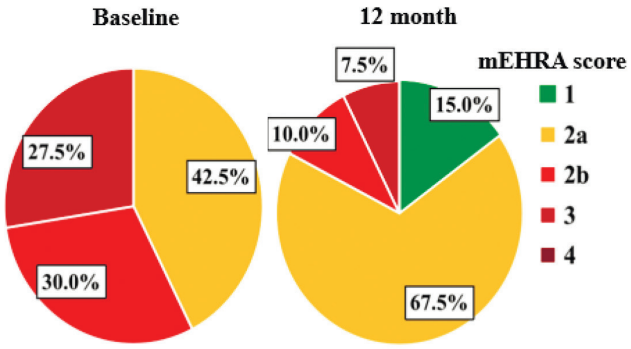

Fig. 3. EHRA grade at baseline and 12 months after cryoballoon ablation in patients with recurrent atrial fibrillation after intervention.

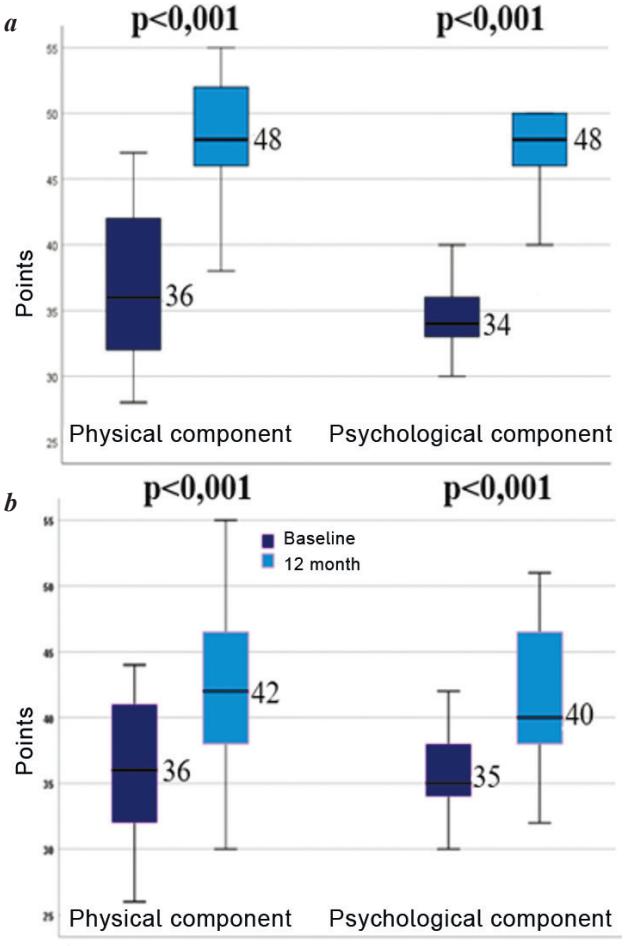

Fig. 4. Dynamics of physical and psychological health component scores on the SF-36 scale at baseline and 12 months after cryoballoon ablation in patients without (a) and with (b) recurrences of atrial fibrillation after the intervention.

The next section of our study was to evaluate arrhythmia-related symptoms and quality of life in patients before the intervention and 12 months after the intervention. In accordance with the obtained data, statistically significant dynamics was observed for all classes of the EHRA scale when comparing baseline values and after 12 months of follow-up: The number of patients with class 3 decreased from 11 (27.5%) patients to 3 (7.5%) (p=0.031), with class 2b from 12 (30.0%) to 4 (10.0%) (p=0.021), while the number of patients with class 2a increased from 17 (42.5%) to 27 (67.5%) (p=0.021). Initially, no patient was categorized as grade 1, and after 12 months, 6 patients had EHRA grade 1 (p=0.008). At both baseline and 12 months, no patients with grade 4 were noted (Fig. 3).

Consistent with these findings, there was a statistically significant increase in the psychological and physical component scores of the SF-36 scale (p<0.001) among patients who had a recurrence of AF after 12 months, regardless of the amount of intervention: from 36.0 points to 42.0 points on the physical component of the SF-36 scale and from 35.0 points to 40.0 points on the psychological component of the SF-36 scale in patients with recurrent AF, and from 36.0 points to 48.0 points on the physical component of the SF-36 scale and from 34.0 points to 48.0 points on the psychological component of the SF-36 scale in patients without recurrent AF. An increase in scores was observed in 82.5% of patients on the physical component of the SF-36 scale and in 80.0% of patients on the psychological component of the SF-36 scale (Fig. 4).

DISCUSSION

In persistent AF, more pronounced electrical and structural remodeling of the LA is observed, especially in the region of the posterior LA wall [7, 8]. These pathologic processes contribute to the substrate that maintains AF and probably causes the insufficient effectiveness of PV isolation in persistent AF. Meta-analyses of several randomized and observational studies have shown some advantages of additional LA posterior wall ablation compared with PV isolation alone for this form of arrhythmia [9-11]. However, the role of additional influences outside of the PV is currently undefined [1].

It is anticipated that successful treatment of persistent AF will be determined by technologies that identify as accurately as possible the «arrhythmogenic substrate» - the non-PV trigger of AF. The concept of «extended» balloon cryoablation involving additional cryo-interventions in the region of the posterior wall of the LA was first proposed by A.Aryana et al. (2018) and is based on the assumption that the sources of AF can be eliminated without their precise electrophysiological and anatomical identification in the absence of technology for mapping of the said «sources» of AF to date [5]. In this study, higher intervention efficacy was observed in the group of patients who underwent cryoablation of the PV and LA posterior wall. In contrast to the work of A.Aryana et al. (2018), our study did not show significant benefits of «extended» LA cryoablation. First,

this may be due to the high-density voltage mapping of the LA performed by the foreign coauthors as part of the same extended cryoablation procedure and the application of additional radiofrequency ablation in the oposterior wall. Thus, according to the results of this work, more than 30% of patients had no electrical isolation in the region of the posterior wall of the LA, in connection with which radiofrequency ablation of this zone was performed to achieve isolation. Despite the lack of significant differences in the efficacy of the two approaches, our results indicate the safety of the extended cryoablation method. Compared to the work of A.Aryana et al (2018), no major complications were reported in both groups in our study.

According to the results of the performed study, the main predictor of AF recurrence in the interval of 3-12 months after CBA is the recurrence of AF/AFt in the blanking period. The obtained data are consistent with the results of earlier studies and meta-analyses indicating the appropriateness of individualized assessment of the risks of AF recurrence after cryoablation in patients with persistent AF [12, 13].

Another aspect of our study was to evaluate arrhythmia-related symptoms and quality of life in patients before and 12 months after intervention in patients with arrhythmia recurrence. After performing CBA, there is a significant improvement in quality of life in both patients without recurrent AF and patients with recurrent AF. In addition, the severity of arrhythmia-related symptoms is reduced in patients with recurrences after performing CBA.

At present, despite the use of modern ablation techniques, no benefit of additional off-PV interventions on improving the efficacy of the intervention has been demonstrated. Arguably, the strategy for the interventional treatment of persistent AF should include investigation of the LA substrate, which is known to be a major factor in the recurrence of AF after intervention. The study of structural changes in LA myocardium according to the data of cardiac magnetic resonance imaging with delayed contrast imaging will allow to improve the strategy of catheter ablation in persistent AF. Early recurrence of AF (in the first 3 months after the intervention) appeared to be an independent risk factor for recurrence of AF in the distant period after CBA in both groups. There was a significant reduction in symptom severity and improvement in quality of life after the intervention in patients with and without recurrent AF.

CONCLUSION

Extended CBA combined with cryoablation of the LA posterior wall is comparable in efficacy to standard PV CBA. The indication for extended CBA should be determined considering potential clinical and instrumental predictors of intervention efficacy. A promising direction is the study of structural changes in LA myocardium according to the data of cardiac magnetic resonance imaging with delayed contrasting. Recurrence of AF/AFl in the blanking period is an independent risk factor for recurrence of AF in the distant periods after intervention. Improvement in quality of life and reduction in the severity of arrhythmia-related symptoms in patients with recurrences may indicate a partial effect of CBA.

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