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Some Echocardiographic Indicators as Probable Predictors of Atrial Fibrillation Recurrence in Patients with Arterial Hypertension after Catheter Ablation

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Abstract

INTRODUCTION: The work is devoted to the study of possible predictors of atrial fibrillation (AF) recurrence after interventional procedures. We conducted a retrospective-prospective, observational, analytical study to analyze the electrophysiological predictors of AF recurrence in patients with arterial hypertension after catheter ablation of the pulmonary veins.

MATERIALS AND METHODS: The study included 150 patients of 62.4 ± 7.47 years mean age. There were 66 women and 84 men, which accounted for 44% and 56%, respectively. Seventy (46.6%) patients with paroxysmal AF, 46 (30.6%) patients had paroxysmal AF, and 34 (22.6%) patients had long-term persistent AF. All of them underwent catheter isolation of the pulmonary veins. According to the effectiveness of ablation, patients were divided into two groups: 103 patients, maintained sinus rhythm for 12 months, and 47 patients with recurrent AF.

RESULTS: As a result of our study, some echocardiographic predictors of AF recurrence were identified. Multivariate correlation analysis revealed a moderate positive relationship between AF recurrence and indicators such as LA area ($r = 0.599$; $p < 0.01$), RA area ($r = 0.479$; $p < 0.01$), LVMMI ($r = 0.557$; $p < 0.01$), LVMM ($r = 0.367$; $p < 0.01$), LV EDD ($r = 0.381$; $p < 0.01$), LV ESD ($r = 0.375$; $p < 0.01$), BMI ($r = 0.596$; $p < 0.01$), weight ($r = 0.285$; $p < 0.01$), heart failure (HF) 0−1 functional class (FC) ($r = 0.201$; $p < 0.01$), and HF 2 FC ($r = 0.192$; $p < 0.01$).

CONCLUSION: This research provides specific clinical and anamnestic data (BMI, weight, HF of NYHA Class I-II) and echocardiographic parameters that are ourstandingly correlated with the development of AF recurrence: these are the areas of the LA and RA, LVMMI, LVMM, LV EDD, LV ESD, concomitant HRD VES and SES, TV regurgitation

Introduction

Atrial fibrillation (AF) is one of the most common and complex arrhythmias and the most common arrhythmia characterized by unstable atrial electrical activity. Data from epidemiological studies have shown that there are more than 33.5 million patients with AF worldwide. Atrial fibrillation may not manifest for a long time and remain without clinical manifestations, which is the reason for the late diagnostics of the disease. The prevalence of AF in the population is 1−2% [1], [2], [3], [4]. The annual detection of AF in the European Union ranges from 120,000 to 215,000 new cases. It is expected that the number of patients suffering from AF will increase to 14−17 million by 2030 [5], [6]. The increase in the prevalence of AF can be explained by the improvement in both the diagnosis of AF and the increase in life expectancy in patients with cardiovascular disease.

Rhythm control with various antiarrhythmic drugs is effective in <30%. Today, catheter ablation is an established method and is more effective than antiarrhythmic drug therapy. The main goal of these methods is to restore and maintain sinus rhythm for a long time [7], [8], [9].

According to the results of studies, AF triggers can be located in different parts of both the left and right atria: A posterior wall of the left atrium, interatrial septum, coronary sinus, and mouth of the superior vena cava. In 72% of cases, ectopic activity is recorded in the upper pulmonary veins. The fundamental goal of ablation methods for patients with AF is to restore the sinus rhythm and maintain it for the long term in a certain category of patients by isolation of arrhythmogenic sites and possibly elimination of arrhythmia substrate [10], [11], [12], [13]. Ablation effectiveness relevance should take into account not only certain electrophysiological functions of the left atrium, the presence and severity of underlying heart disease, but also possible alternatives (antiarrhythmic drugs and rate control) and patient preferences. Thus, an individual approach to catheter ablation of specific AF mechanisms is required, as well as the search for a method to eliminate AF using the least amount of exposure [14], [15].

RF and cryoballoon ablation

Radiofrequency ablation (RFA) is a highly effective interventional treatment for many arrhythmias. In 2015, the results of a global study comparing the efficacy of drug treatment of AF with amiodarone and RFA were presented. Published data have shown the clear efficacy of interventional treatment of this arrhythmia. Thus, 70% of patients after RFA did not have a recurrence of AF for 2 years. In the group with drug treatment of this arrhythmia, the efficiency within 2 years was observed only in 34% of patients. In the analysis of mortality rates and the frequency of indicators in the group of interventional treatment of AF, there were also lower rates. Thus, to date, RFA is effectively used in the treatment of AF, the technical characteristics of which continue to improve.

One of the new directions in interventional arrhythmology is the cryoablation procedure (CBA), which was first performed in 2005 in Europe. Despite the fact that catheter ablation is more effective than antiarrhythmic therapy, AF recurrences are noted.

In general, better efficacy and fewer AF recurrences and other complications can be expected in younger patients with a short history of AF and in the absence of structural heart disease. There may be late returns of AF (after a year of maintaining sinus rhythm) and they occur quite often after catheter ablation, including in patients without structural heart disease and in centers with extensive experience in performing this procedure. According to the literature, relapse of atrial arrhythmia after catheter ablation in patients with paroxysmal AF occurred on average in 24.8% of cases, and with a persistent form in 44.65% [16], [17], [18]. A number of studies have identified some predictors of AF recurrence after catheter ablation methods, but their predictive level is insufficient. In this regard, this issue remains relevant and needs further research [19], [20], [21], [22], [23], [24], [25], [26].

Materials and Methods

The study was conducted on the basis of the National Scientific Cardiosurgical Center in the Department of Arrhythmology.

Criteria for inclusion of patients in the study groups:

1. Patients over 18 years of age
2. Signed informed consent of patients for EPS, CBA, or RFA.
3. Symptomatic paroxysmal, persistent AF resistant to Class I or III antiarrhythmic drugs (or intolerance).

Criteria for exclusion of patients from the study group:

1. Patients under 18 years of age.
2. Decompensation of concomitant diseases
3. Patient's refusal to undergo EPS, CBA, or RFA
4. Thromboembolism of the pulmonary artery (within 6 months).
5. Peptic ulcer of the stomach/duodenal ulcer in the active phase, erosive gastritis/duodenitis/ esophagitis in the presence of erosion.
6. High risk of life-threatening bleeding with contraindications to taking oral anticoagulants.
7. Malignant neoplasms in the terminal stage.
8. Allergic reactions to contrast/iodine-containing substance.
9. Distinct electrolyte disorders. Severe coagulopathy. Severe anemia.

The study included 150 patients of 62.4 ± 7.47 years of mean age with AF in combination with hypertension. All patients underwent catheter isolation of the pulmonary veins. Patients were divided into two groups according to the effectiveness of ablation: 47 patients with recurrent and AF 103 patients remained in sinus rhythm for 12 months. Atrial fibrillation recurrence was documented by ECG, Holter ECG. Heart parameters were assessed according to the European guidelines on echocardiography.

Echocardiographic protocol

Cardiac parameters were evaluated according to the European Echocardiography Guidelines (2018). The echocardiographic protocol was led according to the recommendations for quantification of cameras by the American Society of Echocardiography and the European Association for Cardiovascular Imaging. Echocardiographic measurements were performed by a senior physician certified in echocardiography who was unaware of the clinical data and patient outcomes.

The left ventricular ejection fraction, end-diastolic and end-systolic volumes were evaluated by modified Simpson biplane measurement. LV mass and its indexed values, linked to body surface area in a square meter, were calculated using the formula of Devereux *et al*.

Diastolic filling of the left ventricle was evaluated using pulsed-wave Doppler echocardiography by transmitral flow. The peak velocity of the E wave (early fill wave), the deceleration time of the transmitting Doppler wave E, and the velocity of the peak A wave (late fill wave) were measured. Myocardial velocity in the basal interventricular septum was assessed using pulsed-wave tissue Doppler echocardiography in systole (Sm) and diastole (Em). The E/Em ratio was calculated as a measure of the left ventricular filling pressure. The Valsalva maneuver was used to assess the pseudo-normal type of diastolic myocardial dysfunction. The volume of the left atrium was measured by the biplane Simpson method in the apical four-chamber and two-chamber projections and indexed by body surface area.

Table 1: Characteristics of the studied patients

Characteristic/indicator	All patients (n = 150), n (%)	Group with relapse (n = 47), n (%)	Group without recurrence (n = 103), n (%)	p
Average age, years	62.4 ± 7.47	68.12 ± 4.52	59.8 ± 7.09	0.001
Men	84 (56)	15 (32)	69 (67)	<0.001
Women	66 (44)	32 (68)	34 (33)	
Height, cm	166.05 ± 8.82	162.17 ± 8.25	167.82 ± 8.54	0.0002
Weight, kg	85.21 ± 11.62	90.40 ± 11.75	82.84 ± 10.82	0.0001
BMI	31.15 ± 3.87	34.63 ± 3,49	29.56 ± 2.87	0.001
APT	1.90 ± 0.17	1.84 ± 0.16	1.92 ± 0.17	0.013
AF paroxysmal	70 (46.6)	26 (55.3)	44 (42.7)	0.152
AF persistent	46 (30.6)	10 (21.2)	36 (34.9)	0.093
AF is long-term persistent	34 (22.6)	11 (23.40)	23 (22.33)	0.885
AG 2 degree	51 (34)	9 (19.4)	42 (40.77)	0.010
AG 3 degree	99 (66)	38 (80.8)	61 (59.2)	0.010
IHD HF	43 (28.6)	15 (31.9)	28 (27.18)	0.553
HF NYHA Class 0–I	89 (59.3)	21 (44.6)	68 (66.09)	0.014
HF NYHA Class 2	59 (39.3)	25 (53.19)	34 (33)	0.019
Concomitant HRD VES	58 (38.6)	25 (53.19)	33 (32)	0.014
Concomitant HRD SES	18 (12)	10 (21.2)	8 (7.7)	0.019
Concomitant HRD AF	7 (4.6)	3 (6,8)	4 (3.8)	0.501
Type 2 diabetes	29 (19.3)	17 (36.17)	12 (11.6)	<0.001
Arrhythmic history 0–5 years	66 (44)	10 (21.2)	56 (54.3)	<0.001
Arrhythmic history 5–10 years	58 (38.6)	25 (53.19)	33 (32)	0.014
Arrhythmic history>10 years	25 (16.6)	12 (25.5)	13 (12.6)	0.050
AF recurrence 0–3 months	14 (29.7)			
AF recurrence 3–6 months	12 (25.5)			
AF recurrence 6–12 months	21 (44.6)			

BMI: Body mass index, HF: Heart failure, AF: Atrial fibrillation.

The study conformed to the principles of the Declaration of Helsinki and was approved by the local ethics committee. All patients signed a voluntary informed consent for the study.

Statistical analysis

Statistical analysis was performed using Microsoft Excel 2019, IBM SPSS Statistics for Windows, version 23.0.

Checking quantitative signs for normal distribution in each group of patients were carried out using the Shapiro–Wilk test. Depending on the distribution, a comparison of quantitative indicators was carried out using the Student's *t*-test for independent samples and the Mann–Whitney U-test. Qualitative features were compared using Pearson's Chi-square test and Fisher's exact test. Correlation analysis was performed using the correlation coefficient of Pearson, Spearman, Phi, and Cramer's V.

Results

The study was conducted on the basis of JSC "National Scientific Cardiac Surgery Center" in the Department of Interventional Arrhythmology. The study included 150 patients with a mean age of

Table 2: ECHOCG and ECG data in the studied patients

Characteristic/indicator	All patients (n = 150), n (%)	Group with relapse (n = 47), n (%)	Group without recurrence (n = 103), n (%)	p
QRS (ms)	94.11 ± 12.92	96.27 ± 11.19	93.13 ± 13.57	0.11
QTc	426.52 ± 57.91	417.65 ± 74.0	430.56 ± 48.75	0.23
PQ (ms)	192.05 ± 55.50	224.44 ± 69.62	177.26 ± 40.12	<0.001
LV EDD (mm)	4.68 ± 0.61	5.15 ± 0.55	4.46 ± 0.51	<0.001
Indexed EDD	2.45 ± 0.29	2.60 ± 0.34	2.38 ± 0.23	<0.001
LV ESD (ms)	3.46 ± 0.80	3.97 ± 0.85	3.22 ± 0.65	<0.001
Indexed LV ESD	1.74 ± 0.48	2.03 ± 0.50	1.61 ± 0.37	<0.001
LVMM (g)	180.21 ± 51.61	225.34 ± 44.18	160.29 ± 40.61	<0.001
LVMMI	92.07 ± 23.99	112 ± 19.25	83.30 ± 20.17	<0.001
LV EDV (mm)	95.91 ± 25.69	99.08 ± 30.353	94.62 ± 23.38	0.37
Indexed LV EDV	50.66 ± 12.37	51.96 ± 12.38	50.58 ± 11.38	0.72
LV ESV (mm)	47.75 ± 21.24	43.21 ± 16.93	50.01 ± 22.71	0.085
Indexed LV ESV	25.29 ± 11.95	22.97 ± 10.74	26.55 ± 12.19	0.15
SV (ml)	55.01 ± 15.29	59.51 ± 20.29	53 ± 12.03	0.045
LV EF %	56.42 ± 5.23	53.44 ± 3.94	57.70 ± 5.19	<0.001
Volume LA (ml)	82.77 ± 23.06	100.1064 ± 28.5	74.85 ± 14.44	<0.001
Indexed volume LA (ml/m²)	41.00 ± 8.74	47.27 ± 9.21	38.13 ± 6.85	<0.001
LA area (cm²)	23.80 ± 4.15	26.61 ± 3.37	22.72 ± 3.12	<0.001
Volume RA (ml)	71.27 ± 23.63	93.34043 ± 26.41	61.20 ± 13.21	<0.001
Indexed volume RA (ml/m²)	34.53 ± 12.79	44.93617 ± 14.45	29.78 ± 8.49	<0.001
RA area (cm²)	21.49 ± 3.78	24.34043 ± 4.48	20.18 ± 2.52	<0.001
LA dilatation	53 (35.3)	16 (34)	37 (35.9)	0.824
Dilatation of both atria	44 (29.3)	31 (65.9)	13 (12.6)	0.001
Ascending aortic dilatation	40 (26.6)	34 (72.3)	6 (5.8)	0.001
Dilatation of the sinuses of Valsalva, sinotubular junction	11 (7.3)	10 (21.2)	1 (0.9)	0.001
LVH	89 (59.3)	45 (95.7)	44 (42.7)	0.001
LVDD 1	61 (40.6)	34 (72.3)	27 (26.2)	0.001
LVDD 2	19 (12.6)	10 (21.2)	9 (8.7)	0.033
Pulmonary hypertension	5 (3.3)	3 (6.3)	2 (1,9)	0.160
TV insufficiency	65 (43.3)	29 (61.7)	36 (34.9)	0.003
AoV insufficiency	40 (26.6)	16 (34.04)	24 (1.9)	0.168
MV insufficiency	90 (60)	38 (80.8)	52 (50.4)	0.001

EDD: End-diastolic dimension, LV: Left ventricular, ESD: End-systolic dimension, ESV: End-systolic volume, EDV: End-diastolic volume, EF: Ejection fraction, LA: Left atrial, RA: Right atrial, LVH: Left ventricular hypertrophy.

62.4 ± 7.47 years (Table 1). There were 66 women and 84 men, which accounted for 44% and 56%, respectively. Of these, 70 (46.6%) patients had paroxysmal AF, 46 (30.6%) patients had paroxysmal AF, and 34 (22.6%) patients had long-term persistent AF. All of them underwent catheter ablation of the pulmonary veins. Patients were divided into two groups depending on the results of follow-up: 103 patients maintained sinus rhythm for 12 months and 47 patients had AF recurrence. AH Grade 2 was documented in 33 (28.2%) patients, AH Grade 3 in 84 (71.7%) patients, and IHD was observed in 22 (18.8%) patients. In patients with paroxysmal AF, relapses occurred in 24.2% of cases, with persistent AF in 34.7% and with long-term persistent AF in 41.1%, respectively. It should be noted that between the studied groups, differed statistically was found in such indicators as age, gender, BMI, height, weight, APT, AH, concomitant HRD, and duration of arrhythmia history.

According to the results of an echocardiographic study, the volume of the left atrium (LA) was 100.10 ± 28.5 ml in the first group and 74.85 ± 14.44 ml in the second group ($p < 0.01$), which significantly exceeds the normal values (Table 2). It should also be noted a statistically significant difference between groups ($p < 0.01$), such indicators as the indexed volume of the LA and its area, which amounted to 47.27 ± 9.21 ml/m²; 38.13 ± 6.85 ml/m²; and 26.61 ± 3.37 cm²; 22.72 ± 3.12 cm², respectively. There was a significant difference between the groups ($p < 0.01$) of such indicators as the volume of the right atrium (RA) (93.34 ± 26.41 ml and 61.20 ± 13.21 ml); RA area (24.34 ± 4.48 cm² and 20.18 ± 2.52 cm²). Dilatation of both atria occurred in 44 (29.3%) patients and dilatation of only the left atrium in 53 (35.3%) patients. There were also signs of left ventricular hypertrophy: LVMM in Group 1 was 225.3 ± 44.1, in Group 2, 160.29 ± 40.61 ($p < 0.01$), LVMMI was 112 ± 19.25 and 83.30 ± 20.17, respectively ($p < 0.01$). It should also be noted a significant difference between the groups of such indicators as LV EDD ($p < 0.01$; 5.154 ± 0.55; 4.46 ± 0.51) and LV ESD ($p < 0.01$; 3.97 ± 0.85; 3.22 ± 0.65).

To predict the risk of AF recurrence based on correlation analysis, significant predictors of AF recurrence after catheter ablation methods were obtained (Table 3): LA area ($r = 0.599$; $p < 0.01$), RA area ($r = 0.479$; $p < 0.01$), LVMMI ($r = 0.557$; $p < 0.01$), LVMM ($r = 0.367$; $p < 0.01$), LV EDD ($r = 0.381$; $p < 0.01$), LV ESD ($r = 0.375$; $p < 0.01$), BMI ($r = 0.596$; $p < 0.01$), weight (($r = 0.285$; $p < 0.01$)), concomitant HRD SES ($r = 0.193$; $p < 0.01$), TV insufficiency ($r = 0.284$; $p < 0.01$), HF 0-1 FC ($r = 0.201$; $p < 0.01$), and HF 2 FC ($r = 0.192$; $p < 0.01$). Taking into account the obtained correlation relationships, at the next stage of the study, an ROC curve of the relapse relationship with significant indicators was constructed.

Figure 1 shows the ROC curve of the relationship between recurrence and LA volume. The area under the ROC curve was 0.786 ± 0.045 with 95% CI: 0.679−0.858. Assessing the relationship between AF recurrence and LA area, the area under the ROC curve was 0.783 ± 0.043 with 95% CI: 0.699−0.867.

Table 3: Correlation analysis of possible predictors of atrial fibrillation

Pairs of variables	Correlation coefficient	p
AF recurrence and weight	0.285	0.0001
AF recurrence and BMI	0.596	0.0001
AF recurrence and LVMM	0.367	0.0001
Recurrent AF and LVMMI	0.557	0.0001
AF recurrence and LA area	0.599	0.0001
AF recurrence and AF area	0.479	0.0001
Recurrent AF and concomitant VES	0.288	0.0001
Recurrent AF and concomitant SES	0.193	0.018
AF recurrence and shortness of breath	0.249	0.002
AF recurrence and TV insufficiency	0.284	0.0001
AF recurrence and LV EDD	0.381	0.0001
Recurrent AF and LV ESD	0.375	0.0001
Recurrence of AF and hypertension of the 2nd degree	0.212	0.009
Recurrence of AF and AH of the 3rd degree	0.2	0.009
Recurrent AF and HF 0-1 FC	0.201	0.014
Recurrent AF and HF 2 FC	0.192	0.019

AF: Atrial fibrillation, BMI: Body mass index, LA: Left atrial, EDD: End-diastolic dimension, LV: Left ventricular, ESD: End-systolic dimension, FC: Functional class.

The threshold value of LA volume and area at the cutoff point is 81.5 ml (sensitivity and specificity were 70.2% and 66%) and 24.5 cm² (sensitivity and specificity were 68.1% and 68.9%). If the indicator is equal to or exceeds this value, a high risk of AF recurrence is predicted. The quality of the model for these indicators is good. The resulting model was statistically significant ($p < 0.001$).

The area under the ROC curve corresponding to the relationship between recurrence and PP volume (Figure 2) was 0.894 ± 0.026 with 95% CI: 0.844−0.945. Assessing the relationship between AF recurrence and RA area, the area under the ROC curve was 0.796 ± 0.040 with 95% CI: 0.717−0.875.

The threshold value of RA volume and area at the cutoff point is 69.5 ml (sensitivity and specificity were 89.4% and 76.7%) and 21.5 cm² (sensitivity and specificity were 72.3% and 66.0%). If the indicator

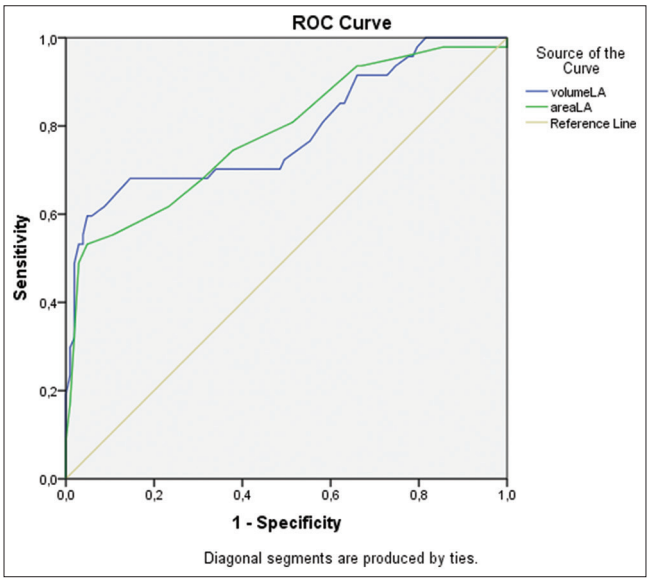

Figure 1: ROC curve of the relationship between recurrence, LA volume, and area

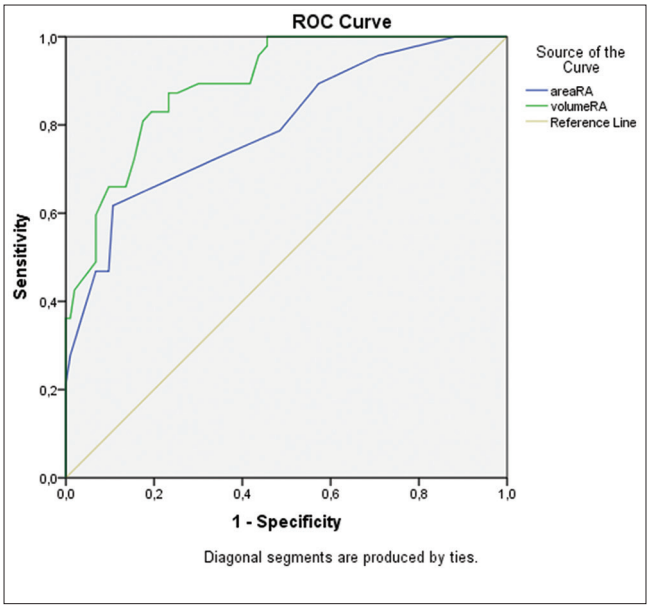

Figure 2: ROC curve of the relationship between recurrence, volume, and area of RA

is equal to or exceeds this value, a high risk of AF recurrence is predicted. The quality of the model for the RA volume is very good, and for the RA area, it is good. The statistical significance of the resulting model was $p < 0.001$.

Discussion

Catheter ablation methods are increasingly being introduced into clinical practice for the treatment of AF against the background of an increase in the number of patients with this severe form of arrhythmia. Meanwhile, the number of patients with persistent sinus rhythm after interventional methods of exposure is also increasing [27].

In this research we were identifying some electrophysiological and ECG parameters as probable predictors of AF recurrence in patients with arterial hypertension after catheter isolation of the pulmonary veins. It should be noted that 47 (31.3%) of 150 patients had a recurrence of AF. The median time to recurrence of AF after ablation was 1−3 months. This observation is consistent with the process of reverse atrial electrical remodeling after the restoration of sinus rhythm. During this reverse electrical remodeling phase, the atrium is at an increased risk of AF recurrence. In our study, we studied echocardiographic predictors of AF recurrence. Using the methods of multivariate statistical analysis, certain predictors of AF recurrence were identified: LA area, RA area, LVMMI, LVMM, LV EDD, LV ESD, BMI, weight, concomitant HRD VES and SES, TV insufficiency, and HF of NYHA Class I−II. The results obtained are consistent with the opinion of other researchers. Thus, in a multivariate analysis, Bollmann *et al*. found that the left atrial area obtained by echocardiography can predict early recurrence of AF in patients with persistent AF. Olshansky initials *et al*. reported that in the AFFIRM study, the left atrial diameter correlated with AF recurrence. In the SPAF-I and -II studies, AF recurrence was predicted based on age, presence of congestive heart failure, prior myocardial infarction, and left atrial diameter.

Based on the data of domestic and foreign authors, as well as the results of our study, we can conclude that catheter ablation methods are effective and safe methods of treating patients with AF.

Conclusion

1. A 2-year follow-up of 150 patients who underwent CBA or RFA showed AF recurrence in 47 patients, which was 31.3%. Of these, relapse occurred in 29.7% of patients in the first 3 months, in 25.5% of patients within 6 months, and in 44.6% of patients after 6 months.
2. We have identified clinical and anamnestic data (BMI, weight, and HF of NYHA Class I-II) and echocardiographic parameters that are significantly correlated with the development of AF recurrence: These are the areas of the LA and RA, LVMMI, LVMM, LV EDD, LV ESD, concomitant HRD VES and SES, and TV regurgitation.
3. One of the possible options for the selection of patients with AF for CBA or RFA is the use of a model with the inclusion of some clinical and echocardiographic parameters that can be possible predictors of AF recurrence at various times after catheter ablation methods. It should be noted that it is not possible to accurately predict the timing of the development of AF recurrence, but it can be concluded that there is a relationship between some echocardiographic parameters, their severity, and the development of AF recurrence at different times after catheter ablation methods.

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