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PREDICTORS OF EARLY ARRHYTHMIA RECURRENCE AFTER ATRIAL FIBRILLATION CATHETER ABLATION

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Aim. Search for predictors of early recurrence of atrial tachyarrhythmias after radiofrequency ablation (RFA) of atrial fibrillation (AF).

Methods. The study included 57 subjects with persistent (n = 17; 30%) and paroxysmal (n = 40; 70%) forms of AF, admitted for the RFA. All patients underwent transthoracic echocardiography, assessment of deformation of both atria using 2D Strain, computed tomography (CT) with 3D reconstruction of the left atrium (LA). Intraoperatively, high-density voltage mapping of LA was performed before RF pulmonary vein isolation. All patients underwent follow-up after 3 months.

Results. Recurrence of atrial tachyarrhythmia after 3 months was recorded in 17.5% of patients. High prevalence of low-amplitude activity zones in the LA and persistent AF were the strongest predictors. The LA reservoir function below 21.7%, the conduction function below 15.7%, the LA stiffness index above 0.314 relative units, the LA volume with the appendage above 121.7 ml, and the LA vertical size according to CT data above 65.5 mm statistically significantly predicted early recurrences of atrial tachyarrhythmias with high sensitivity and specificity.

Conclusion. The decreased LA deformation in the reservoir and conductor phase, increased LA stiffness index, the prevalence of low-amplitude activity zones, vertical size and volume of the LA with an auricle according to CT data and persistent AF are significant predictors of early relapses after interventional treatment of AF.

Key words: atrial fibrillation; catheter ablation; left atrium; right atrium; atrial fibrosis; atrial deformation; high density mapping.

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Atrial fibrillation (AF) is a widespread cardiac pathology, and its incidence is predicted to increase in the coming decades. This rise is expected to contribute to higher rates of disability and cardiovascular mortality among the adult working population [1]. The cardiology community is focused on identifying medical and surgical treatment methods that can reduce the progression of AF and eliminate this type of arrhythmia in patients [2]. In many arrhythmology centres, catheter ablation (CA) is the primary treatment method for AF, including as a first-line therapy. However, despite advancements in interventional techniques, the recurrence rate of arrhythmias, particularly early recurrences, remains significant [3].

When determining the treatment strategy for an AF patient, clinicians evaluate factors such as left ventricular (LV) systolic function, the presence of valvular pathology, atrial size, volume, and volume index, among others. Yet, even in the absence of significant structural heart changes, early recurrences of atrial tachyarrhythmias frequently occur during the three-month “blanking” period following CA or immediately after its completion, often persisting during subsequent follow-up [4, 5].

Atrial remodelling during AF is characterized by altered contractility and elasticity of myocardial fibres, which may precede structural changes detectable through imaging modalities like echocardiography (Echo) or computed tomography (CT) [6]. The Speckle Tracking Imaging (STE) 2D Strain ultrasound technology enables the assessment of myocardial mechanical function. Numerous studies have demonstrated the predictive value of left atrial (LA) deformation during the reservoir phase in forecasting CA outcomes [7].

In recent years, high-density electrophysiological voltage mapping, an intraoperative method for indirectly assessing myocardial fibrosis, has been increasingly adopted in clinical practice. This technique analyses the amplitude of bipolar signals from atrial tissue. International studies have shown that this technology can predict CA outcomes [8] and provide a personalized approach to arrhythmia substrate modification [9]. Thus, the search for more sensitive predictors of early post-CA recurrences, which would allow for an individualized approach to catheter-based and pharmacological treatment in different patient categories, remains a pressing issue in the scientific cardiology community.

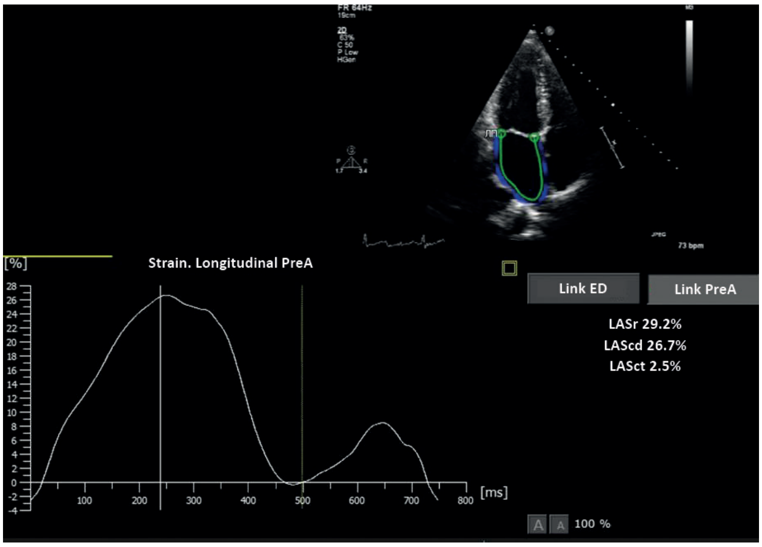

Figure 1. Longitudinal deformation of the left atrium. Note: LAScd - conductor function; LASct – contractile function; LASr – reservoir function;

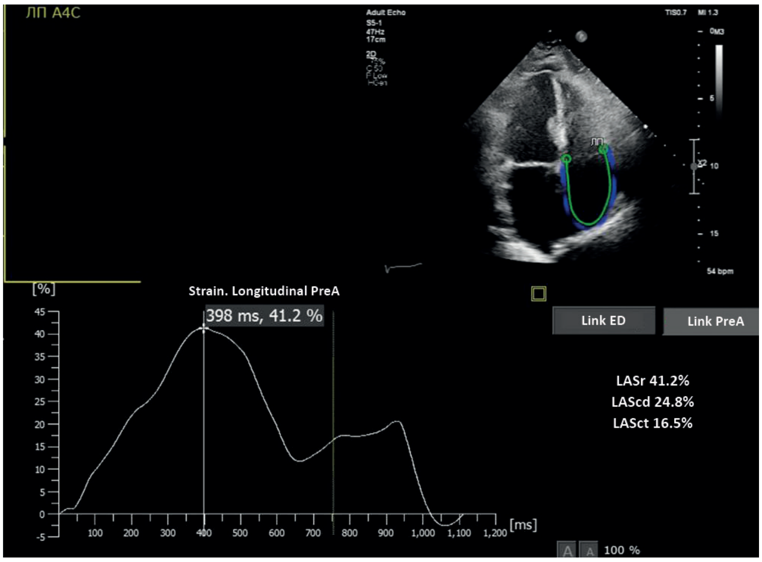

Figure 2. Longitudinal deformation of the right atrium.

Aim. To identify predictors of early recurrences of atrial tachyarrhythmias after radiofrequency ablation (RFA) of atrial fibrillation.

METHODS

A single-centre, prospective, observational, non-randomized study was conducted. The study considered patients admitted to the Department of Surgical Treatment for Complex Cardiac Rhythm Disorders and Electrostimulation at the Cardiology Research Institute, Tomsk, for RFA of AF. Patients with prior RFA for any arrhythmia, valvular, coronary, or congenital heart pathologies, implanted devices, LV contractility impairment (ejection fraction [EF] below 50%, hypo- or akinesia), pulmonary arterial hypertension, or contraindications for RFA were excluded. Ultimately, 57 patients with paroxysmal (n=40; 70%) and persistent (n=17; 30%) forms of AF were included in the study, with a mean age of 55.4±9.8 years.

The study was conducted in accordance with clinical guidelines and the principles of the Declaration of Helsinki. Study protocol No. 205 was approved by the Biomedical Ethics Committee of the Cardiology Research Institute on December 8, 2020. All participants provided informed consent.

During hospitalization, in addition to standard clinical and instrumental examinations, CT with three-dimensional reconstruction of the LA was performed using a 64-detector CT scanner (GE Discovery NM/CT 570c, GE Healthcare, Milwaukee, WI, USA).

The deformation of both atria was assessed in all patients using transthoracic 2D Strain Echo from a four-chamber view on sinus rhythm with a Philips Affinity ultrasound scanner (USA). The P wave was used as the zero value. Image analysis was conducted offline with the Philips QLAB 15 software (USA). Endocardial and epicardial boundaries were manually marked at the end-systole of the LV and right ventricle, determined by the program. After confirmation, a longitudinal strain curve was constructed, including the peak longitudinal positive strain of the right atrium (Fig. 1) and the reservoir phase (positive strain at the end of LV systole), conductor phase (early diastole after mitral valve opening), and

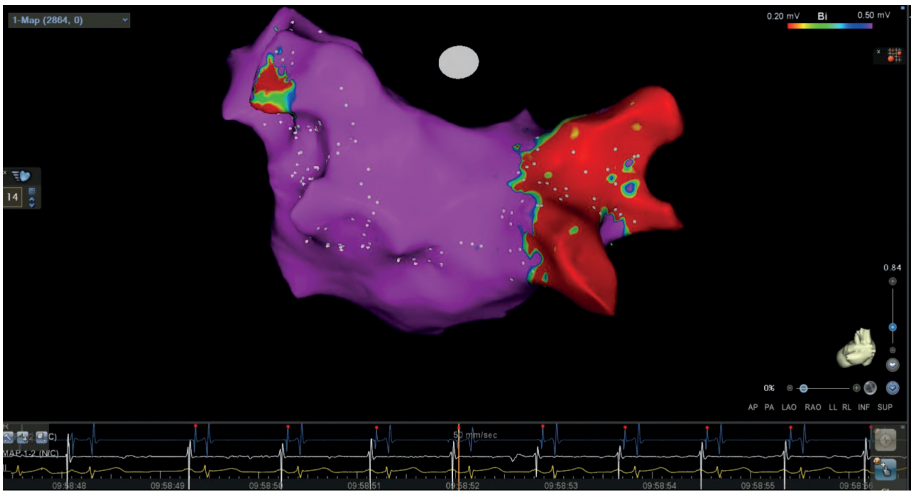

Figure 3. Electroanatomic voltage map of the left atrium, where the low-amplitude zone (less than 0.2 mV) is marked in red (area between the right pulmonary veins).

contractile phase (negative strain during LV end-diastole) of LA strain (Fig. 2). The mean value across all segments was used as the final value [10]. Additionally, the left atrial stiffness index (LASI)—the ratio of E/E′ to global peak LA strain was calculated, reflecting increased filling pressures in the left heart chambers and indirectly indicating LA rigidity and fibrosis [11].

In the X-ray operating room, under intravenous sedation, high-density intracardiac voltage mapping of the LA was performed for all patients using a 20-pole PentaRay catheter (Biosense Webster Inc.) in sinus rhythm. Bipolar voltage maps were recorded and filtered at a frequency of 30-300 Hz, containing at least 3,000 points. Low-voltage zones were defined as areas with three or more points with a bipolar signal amplitude of less than 0.2 mV (Fig. 3). The CARTO 3 non-fluoroscopic system (Biosense Webster, USA) was used for the electroanatomical reconstruction of the LA [12].

Next, RFA with pulmonary vein (PV) isolation was performed using a NaviStar CoolFlow or SmartTouch ThermoCool ablation catheter (Biosense Webster, USA). The criterion for electrical isolation of the PVs was the disappearance of potentials on the circular Lasso electrode (Biosense Webster, USA) and confirmation of bidirectional conduction block during control pacing [13].

Following RFA, all patients received antiarrhythmic, anticoagulant, and therapy for underlying pathologies per clinical guidelines [1]. Follow-up was conducted three months after the RFA during a “blanking” period, during which patients’ clinical conditions were assessed. Recurrence was defined as atrial tachyarrhythmias documented on an electrocardiogram (ECG) or 24-hour Holter ECG monitoring lasting more than 30 seconds and occurring during the three-month blanking period or persisting beyond its end. Based on the data analysis, patients were divided into two groups according to the presence of atrial tachyarrhythmia recurrence: Group 1 - without recurrence, and Group 2 - with recurrence within three months after RFA.

Statistical analysis

Statistical analysis was performed using SPSS Statistics 26 (IBM Corporation, USA). The normality of distribution was checked using the Shapiro-Wilk test. Data were described as means with standard deviations (M±SD), medians with interquartile ranges (Me [Q25; Q75]), or absolute values with their percentages. Differences between independent samples were assessed using the Student’s t-test or nonparametric Mann-Whitney U test. For paired samples, the paired Student’s t-test was used, and for nominal indicators, the Pearson χ^2 test was applied. Logistic regression analysis was used to evaluate the prognostic significance of the methods. To compare the diagnostic efficacy of the methods studied in the work, Receiver Operating Characteristic (ROC) analysis was conducted. The informativeness of the diagnostic test was determined by calculating the area under the ROC curve (AUC) and finding the optimal cut-off value. Changes were considered statistically significant at a significance level of p<0.05.

RESULTS

During the 3-month follow-up period after RFA, atrial tachyarrhythmia recurrence was recorded in 10 patients, classified into the second observation group. Among these cases, ECG findings identified AF in seven patients, atrial tachycardia in two, and atrial flutter in one. The groups were comparable regarding sex, age, BMI, cardiovascular pathology, and arrhythmia duration, but patients with recurrence more often exhibited persistent AF (p=0.002). First-class antiarrhythmic drugs (propafenone, etacizine, or lappaconitine hydrobromide) were more frequently used in Group 1, whereas Group 2 predominantly received amiodarone (p=0.008). The clinical characteristics are presented in Table 1.

Table 1.

Clinical characteristics of patients, M±SD or Me [Q25;Q75]

Indicator	Group 1 (n=47)	Group 2 (n=10)	P
Men, n (%)	25 (53)	6 (60)	0.695
Age, years	54.9±10.2	58.1±6.92	0.344
BMI, kg/m²	29.8±5.33	30.3±6.36	0.801
Hypertension, n (%)	42 (89)	9 (90)	0.952
Coronary Artery Diseases, n (%)	14 (29.8)	4 (40)	0.528
Myocarditis, n (%)	2 (4.3)	1 (10)	0.460
Idiopathic AF, n (%)	4 (8.5)	0 (0)	0.339
Paroxysmal AF, n (%)	37 (79)	3 (30)	0.002
Persistent AF, n (%)	10 (21)	7 (70)	
AF Duration, months	12 [7.5; 48]	36 [14; 84]	0.269
CHF I FC, n (%)	7 (14.9)	1 (10)	0.686
CHF II FC, n (%)	5 (10.6)	2 (20)	0.413
EHRA, points	2 [2;2]	2 [1;2]	0.051
CHA_2DS_2-VASc, points	2 [1; 2]	3 [1; 4]	0.244
HAS-BLED, points	0 [0;0]	1 [0;1]	0.250
Antiarrhythmic Therapy*			
Amiodarone, n (%)	9 (19.1)	6 (60)	0.008
Sotalol, n (%)	15 (31.9)	2 (20)	0.455
Class 1C drugs, n (%)	23 (48.9)	2 (20)	0.094
β-blockers, n (%)	1 (2.1)	0 (0)	0.642
Anticoagulant Therapy			
Rivaroxaban, n (%)	18 (38.3)	2 (20)	0.271
Dabigatran, n (%)	8 (14)	4 (40)	0.106
Apixaban, n (%)	21 (44.5)	4 (40)	0.786

Note: hereinafter, BMI - Body Mass Index; AF - Atrial Fibrillation; CHF - Chronic Heart Failure; FC - Functional Class; CHA_2DS_2-VASc - Stroke Risk Score for Patients with AF; EHRA - European Heart Rhythm Association Score for Symptoms Associated with AF; HAS-BLED - Bleeding Risk Score for Patients with AF.

Echo comparisons revealed statistically significant differences: patients with recurrence showed larger vertical dimensions of both atria and higher LA volumes compared to those without recurrence. There were no significant intergroup differences in diastolic or systolic functions or LV size parameters. 2D Strain data indicated that LA deformation in the reservoir and conduction phases was higher in patients maintaining sinus rhythm, while the LA stiffness index was lower compared to Group 2. Right atrial (RA) deformation did not differ significantly between groups (Table 2).

CT findings showed that patients with atrial tachyarrhythmia recurrence had significantly larger LA volumes with appendage (137.2±21.2 ml vs. 109.1±22.8 ml, p=0.001), without appendage (119.5±21.2 ml vs. 100.0±20.7 ml, p=0.010), and vertical size (71.0 [65; 75.4] mm vs. 48.7 [41.0; 66.0] mm, p=0.023).

Table 2.

Echocardiographic characteristics of patients, M±SD or Me [Q25;Q75]

Indicator	Group 1 (n=47)	Group 2 (n=10)	P
LV EF, %	67.0 [64.0; 69.0]	67.0 [64.0; 72.0]	0.636
LV EDV, ml	98.3±18.1	99.0±18.1	0.916
LV ESV, ml	33.0 [27.0; 37.0]	32.0 [24.0; 40.0]	0.898
LV EDI, ml/m²	50.5±5.97	47.8±6.30	0.201
LV ESI, ml/m²	16.7 ±3.16	15.6 ±3.55	0.321
LA APD, mm	39.5±3.50	41.1±4.36	0.199
LA Transverse Dimension, mm	43.0 [41.0; 44.0]	44.5 [41.0; 49.0]	0.163
LA Vertical Dimension, mm	53.4±4.09	57.0±4.47	0.016
LAV, ml	67.1 ±15.9	80.1±21.9	0.034
LAVI, ml/m²	34.9±6.12	38.5±9.00	0.133
RA Transverse Dimension, mm	42.0 [40.0; 44.0]	43.0 [41.0; 47.0]	0.161
RA Vertical Dimension, mm	50.8±3.79	53.5±3.98	0.045
RAV, ml	68.3 [53.0; 74.2]	68.9 [66.0; 90.7]	0.157
RAVI, ml/m²	32.5±5.45	35.6±6.70	0.121
RVSP, mmHg	27.0 [25.5; 29.0]	27.0 [25.0; 30.0]	0.831
LV MMI, g/m²	81.0 [75.0; 85.0]	82.5 [75.0; 91.0]	0.443
E, cm/s	67.0 [60.5; 79.5]	69.5 [58.0; 80.0]	0.975
A, cm/s	70.5±14.7	71.4±5.41	0.840
E/A	0.87 [0.80; 1.25]	0.93 [0.83; 1.08]	0.925
e', cm/s	11.0 [9.00; 12.6]	10.0 [8.90; 11.5]	0.474
E/e'	6.52±1.38	7.08 ± 1.71	0.267
LA Reservoir Function, %	27.5 [24.8;30.0]	19.9 [18.3; 21.1]	0.002
LA Conduction Function, %	17.1 [14.0;20.3]	12.9 [10.4; 15.7]	0.033
LA Contractile Function, %	9.51±3.89	7.97±3.45	0.255
RA Longitudinal Strain, %	28.2±5.81	26.1±6.71	0.306
LA Stiffness Index, rel.u	0.235 [0.198; 0.289]	0.355 [0.266; 0.434]	0.007

Note: hereinafter, EDV - End-Diastolic Volume; ESV - End-Systolic Volume; LV - Left Ventricle; LA - Left Atrium; LAVI - Left Atrial Volume Index; LAV - Left Atrial Volume ; APD - Anterior-Posterior Dimension; RA - Right Atrium; RAVI - Right Atrial Volume Index; RAV - Right Atrial Volume; RVSP - Right Ventricular Systolic Pressure ; EF - Ejection Fraction; E peak - Early Diastolic Filling (Passive Filling Phase); A peak - Late Diastolic Filling (Active Filling Phase); E/A - Ratio of Passive to Active Filling Phases; e' - Velocity of Lateral Mitral Annular Motion (Tissue Doppler); E/e' - Ratio of Passive Filling Phase to Lateral Mitral Annular Velocity.

High-density voltage mapping identified low-amplitude activity zones in 19 patients. These were categorized into four subgroups: 1 (n=38) without low-amplitude zones in the LA, 2 (n=9) with zones covering <20% of LA area, 3 (n=5) with zones covering 20-30%, and 4 (n=5) with zones covering >30% of LA area. Persistent sinus rhythm was less frequently associated with low-amplitude activity zones (75% vs. 30%, p=0.007), and when present, the zones tended to be smaller. Most patients with atrial tachyarrhythmia recurrences belonged to subgroups with more extensive LA involvement.

Univariate and multivariate logistic regression analyses were conducted to assess predictors of early recurrences of atrial tachyarrhythmias after CA, focusing on parameters that showed statistically significant differences between groups (Table 3). Multivariate analysis highlighted persistent AF, the extent of low-amplitude activity zones, reservoir function, LA vertical size, and LA volume with appendage as the strongest predictors. Each predictor's significance was further evaluated using ROC analysis.

LA deformation during the reservoir phase demonstrated a significant inverse association with early recurrences (p=0.002), with an AUC of 0.807±0.091 (95% CI: 0.630-0.985). Patients with deformation <21.7% exhibited a high risk of recurrence, with 80% sensitivity and 91.5% specificity (Fig. 4).

LA volume with appendage showed a direct significant association (p=0.003), with a cut-off value of 121.8 ml (70% sensitivity and 71.4% specificity), characterized by an AUC of 0.806±0.074 (95% CI: 0.661-0.951) (Fig. 5).

CT-based LA vertical size was directly associated with recurrence risk (p=0.023), with a cut-off of 65.5 mm (71% sensitivity and 73% specificity), characterized by an AUC of 0.783±0.127 (95% CI: 0.661-0.951) (Fig. 5).

Although the LASI was not included in multivariate analysis, ROC analysis showed a direct association with early recurrences (p=0.003). The ROC curve demonstrated an AUC of 0.774±0.093 (95% CI: 0.592-0.957) (Fig. 5). LASI >0.314 relative units predicted recurrence risk with 70% sensitivity and 83% specificity.

Similarly, conduction-phase LA deformation exhibited a significant inverse association with recurrences (p=0.033), characterized by an AUC of 0.716±0.096 (95% CI: 0.527-0.904) (Fig. 4). A deformation level <15.8% predicted high recurrence risk with 80% sensitivity and 63.8% specificity.

Three months post-CA, patients with early atrial tachyarrhythmia recurrences exhibited lower LA reservoir function (22.3% vs. 26.6%, p=0.004) and reduced RA longitudinal positive deformation (26.8% vs. 31.4%, p=0.036). These findings reflect ongoing atrial remodeling despite CA and may predict the persistence of arrhythmias beyond the blanking period, potentially necessitating repeat interventions.

DISCUSSION

In clinical practice, the development of atrial tachyarrhythmia paroxysms within the first three months after catheter treatment, the so-called "blanking period," is not considered indicative of an ineffective ablation. This can be attributed to inflammation, alterations in the autonomic nervous system functioning, and/or immaturity of the postoperative scar [3]. However, studies in the global literature have demonstrated the high prognostic value of early atrial arrhythmia recurrences, particularly during the third month after RFA, in predicting long-term CA outcomes [4, 5]. This evidence suggests the need to reconsider the timeframe for evaluating the expected effects of interventional AF treatment.

Predicting the risk of early recurrences for each patient may serve as a basis for individualized approaches to selecting interventional treatment methods and scope, as well as determining the intensity and duration of postoperative antiarrhythmic and anticoagulant therapies. Established predictors of unfavorable outcomes, including early and late recurrences after CA, include factors such as age, obesity, severe cardiovascular pathology, AF type and duration, and significant structural heart alterations [14]. In this study, no significant clinical or demographic differences were observed between groups. However, atrial tachyarrhythmia recurrences were more frequent in patients with persistent AF, regardless of arrhythmia duration.

Patients with arrhythmia recurrences had larger vertical dimensions and LA volumes on Echo and CT, both considered established predictors of CA effectiveness. Interestingly, there were no intergroup differences in anterior-posterior LA size or LA volume index [15].

The pathophysiological basis of atrial remodeling involves myocardial replacement by fibrotic tissue. According to a meta-analysis by Kh. Ghafouri et al. based on 24 studies, the most predictive parameter for CA effectiveness was quantified LA fibrosis from cardiac MRI data: a 10% fibrosis increase was associated with a 1.54-fold higher recurrence rate of AF (95% CI: 1.39-1.70, I^2=50.1%) [18]. Low-amplitude activity zones on intraoperative voltage mapping visualize and quantify fibrotic substrates, with results comparable to cardiac MRI data, as confirmed by a meta-analysis including 22 studies conducted by G.Bijvoet et al.

In this study, the extent of low-amplitude activity zones was categorized based on LA involvement, consistent with domestic and international research [8, 12]. Analysis revealed that low-amplitude activity was more frequent in patients with early recurrences, with greater zone extent emerging as the most significant predictor of early atrial tachyarrhythmia recurrence after CA. Similar findings were reported by E.V. Dedukh et al., where logistic regression analysis identified widespread low-amplitude zones (covering >20% of the LA area, p=0.026) as independent predictors of AF recurrence [12].

Our study focused on atrial deformation parameters, indirectly reflecting myocardial functional status during remodeling. Many researchers have validated the prognostic significance of LA deformation during the reservoir phase [7]. However, few studies, particularly in domestic literature, have assessed the contributions of each LA deformation component (reservoir, conductor, and contractile phases) to CA outcome prediction. Globally, only a few studies, such as that by A.V. Nielsen et al., have an-

Table 3.

Relation of factors to the risk of recurrence of atrial tachyarrhythmias after 3 months

Indicator	Univariate analysis		Multivariate analysis	
	OR; 95% CI	p	OR; 95% CI	p
Persistent form of AF	8.63; 1.88-39.6	0.005	7.47; 1.62-34.4	0.010
LA vertical size (Echo)	1.26; 1.03-1.54	0.012	-	-
RA vertical size (Echo)	1.22; 0.997-1.49	0.53	-	-
LA volume (Echo)	1.46; 1.00- 1.09	0.027	-	-
LA volume without appendage (CT)	1.05; 0.996-1.10	0.037	-	-
LA volume with appendage (CT)	1.06; 1.02-1.11	<0.001	1.05;1.01-1.10	0.017
LA vertical size (CT)	1.09; 1.00-1.19	0.013	1.35; 1.05-1.72	0.018
LA reservoir function	0.747; 0.618-0.904	<0.001	0.772; 0.630-0.943	0.012
LA conductive function	0.838; 0.700-1.00	0.028	-	-
LA stiffness index	1.01; 1.00-1.02;	0.011	-	-
Presence of low-amplitude activity zones	6.81; 1.51-30.6	0.011	-	-
SP of low-amplitude activity zones	2.96; 1.49-5.89	0.001	2.65; 1.21-5.79	0.018

Note: hereinafter, CT - computed tomography; AF - atrial fibrillation; SP - spread percentage alyzed this aspect. In a cohort of 678 patients with various AF types, LA contractile function was the strongest independent predictor of recurrence after CA (odds ratio 1.07, 95% CI: 1.01-1.12, p=0.012) with a threshold value of 11.1% [16]. In our research, significant predictive value was demonstrated for both the LA reservoir and conductor functions.

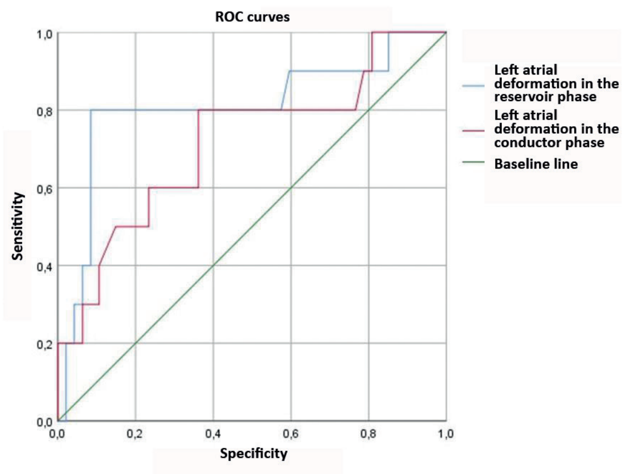

Figure 4. Indicators showing an inverse relationship with the likelihood of early recurrences of atrial tachyarrhythmias after catheter ablation.

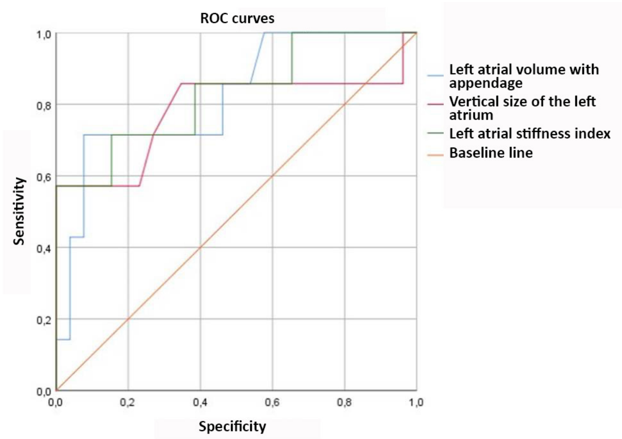

Figure 5. Indicators showing a direct relationship with the likelihood of early recurrences of atrial tachyarrhythmias after catheter ablation.

Our study also demonstrated the high prognostic value of the LA stiffness index, based on longitudinal deformation, reflecting LA rigidity and fibrosis. Similar results were previously reported by I.M. Khurram et al. [17], where patients with long-term atrial tachyarrhythmia recurrences (10.4±7.6 months follow-up) had a higher LA stiffness index (0.83±0.46 vs. 0.40±0.22, p<0.001). However, this index had not been previously evaluated for early recurrences after CA.

Thus, assessing LA deformation and calculating the LA stiffness index preoperatively may allow for a more justified approach to AF treatment strategies and evaluating the need for repeat interventions in cases of early or late atrial tachyarrhythmia recurrences. Given that patients with early recurrences more often exhibited persistent AF and larger low-amplitude activity zones on intraoperative voltage mapping, individualized approaches to arrhythmia substrate modification, expanding LA ablation scope, could be considered for these patients.

Study limitations

The limitations of this study include the small number of patients in the observation groups, the lack of categorization of patients based on the timing of the first atrial tachycardia paroxysm after RFA, and the reliance on interviews and the analysis of submitted ECGs and Holter monitoring data for information on recurrences. The absence of implanted ECG monitoring systems reduces the reliability of the recurrence data.

CONCLUSION

According to our study, early recurrences occurred in 17.5% of patients. A high degree of low-amplitude activity in the LA based on high-density voltage mapping and the presence of persistent AF, regardless of the duration of arrhythmia history, were identified as the strongest independent predictors of early atrial tachyarrhythmia recurrences. A reduction in LA deformation during the reservoir phase below 21.7% and during the conductor phase below 15.7%, an increase in the LA stiffness index above 0.314 relative units, an LA volume with the appendage exceeding 121.7 ml, and an LA vertical size above 65.5 mm on CT imaging predict the risk of early recurrences with high sensitivity and specificity.

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