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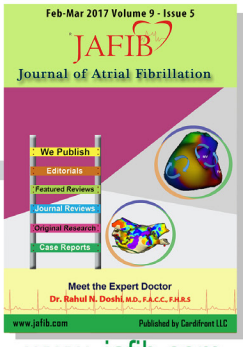

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Comparison of Initial LA Patterns as The Road to Successful Endocardial Box Lesion Ablation

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Abstract

Atrial fibrillation (AF) is the most common arrhythmia in the population. Still there is no unity in understanding of mechanisms and their influence on catheter ablation results. In our study we tried to evaluate accurate initial quantitative indicators of electromechanical remodeling that can border patients from expected good to expected poor results of catheter ablation. We performed electroanatomical mapping and ablation procedures in 94 patient (45 female) in 2012 with 3-year follow-up period. The target points were left atria surface area, complex fragmentation atrial electrograms (CFAE) duration and surface area. We investigated primary procedure efficacy and initial preoperative patterns of patients in sinus rhythm after 3-year follow-up. Patients with paroxysmal AF had about 3-4 such areas with the median duration of fragmentation 84,5 msec and area 10,4 cm^2. In persistent AF were 5-6 zones, duration of 149 msec and area 22,95 cm^2. In long standing (LS) persistent AF 6-9 zones with duration up to 200 msec and area close to 30 cm^2. General efficacy of radiofrequency ablation (RFA) in paroxysmal group was 58,8%, in persistent 33,3% and in LS persistent 12,9% according to Kaplan-Meyer curve with p=0,001. Retrospectively we found that every index in AF recurrence group was 1,5-2 times higher than its equivalent in sinus group. LA surface area was 131,8 cm^2 vs 103,7 cm^2 respectively. Median CFAE duration in AF patients was 157 msec and 87,5 msec in sinus patients. The principal index of CFAE square area was 2,5 times bigger (24,6 cm^2 vs 10,3 cm^2 relatively). We concluded that parameters of mechanical (LA volume and surface area) and electrical (CFAE duration and surface area) remodeling have to be defining in tactics and prognosis of catheter ablation in different types of AF. In order to achieve higher efficacy we advise to use stepwise tactic.

Introduction

Atrial fibrillation (AF) still appears to be the most challenging form of cardiac arrhythmias. There are different strategies for treating this cardiac disorder i.e. from drugs and defibrillation to intervention and open-heart surgery [1]. We will have drastically differing results, especially when comparing surgery and catheter ablation.

Several authors describe efficacy of different types of RFA in various groups of patients. Mean percentage of people in sinus rhythm range from 15% to 88% after primary or secondary procedure [2]. But still in practical guidelines we can see only recommendations for treating AF according to it forms [3].

That's why despite the great variety of published articles no one can provide clear recommendations and values of heart indexes, which are extremely substantial to gain success in interventional treaments of AF. In this article we tried to evaluate accurate initial quantitative indicators of electromechanical remodeling that can border patients from expected good to expected poor results of catheter ablation.

Material and Methods

Study population

The ablation procedures were performed in 2012 with a subsequent 3 years follow-up. The overall population consisted of 94 patients (49 male and 45 female) with different forms of AF: 34 paroxysmal, 30 persistent and 30 long standing (LS) persistent. Among them 41 patients had a moderate functional mitral regurgitation, 22 patients had not significant ischemic heart disease and NYHA class less than 2. All patients had documented AF on ECG and Holter. Previously they were treated with beta-blockers and amiodarone as the main antiarrhythmic therapy (AAT) and with warfarin as the anticoagulation drug. All AAT was canceled before RFA procedure at different times: a week in case of b-blockers and not less then 40 days in case of amiodarone. We used bridge anticoagulation therapy within two days before and after the procedure.

Design

This is a prospective cohort study. The main goals were definition of degree of electromechanical remodeling and efficacy and recurrence risk after RFA. Primary endpoints were recurrence of AF, stroke, different cardiac events (myocardial infarction, surgical operation and others) and death. Secondary endpoint was the end of 3-year follow-up. Patients were divided into 3 subgroups according to the form of AF. All of them underwent three types of RFA: lone pulmonary veins isolation (PVI), PVI with additional CFAE applications and endocardial modification of epicardial "box lesion" set. An electroanatomical mapping with CFAE evaluation was performed in all cases before ablation. Retrospective analysis of initial pattern was performed after reaching the endpoints, either primary or secondary. Patients were divided in two groups according to presenting sinus rhythm in the end of primary study. The basic aims were identification of primary structural and electrical parameters of the heart, which can influence on reverse atrial modeling and design of therapeutic algorithm on this cohort of patients.

Key Words

Endocardial ,Ablation,Atrial Fibrillation

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Diagnostics

Patients from the study underwent Echo and Cardiac computer tomography (CT) routinely before the procedure. Echo was performed with the HP SONOS 5500 (Hewlett Packard Company, Palo Alto, CA, USA) and GE Vivid S5 (GE Healthcare, General Electric, Fairfield, CT, USA) devices. 2D systolic and diastolic parameters of the heart were measured by the Teichholz method. M- and B-modes were used to evaluate conditions of valves, local kinetics and contractility of myocardia and overall hemodynamic. CT was performed on Philips Brilliance CT (Koninklijke Philips N.V., Amsterdam, Netherlands) device. It included pinpoint contrasty scans of left atria (LA) with pulmonary veins (PV) and appendage (LAA) in three dimensions with calculated volumes.

Table 1: Baseline characteristics of all groups of patients

Parameter	Paroxysmal group	Persistent group	LS persistent group	P
Age, y	51.91±11.49	55.83±7.87	56,1±11,66	0.217
Gender (m/f)	15/19	20/10	14/16	-
AF duration, month	11.57±4.13	22.67±8.84	39.98±12.44	0.001
LVED, cm2	5.17±0.56	5.36±0.59	5.2±0.45	0.341
EDV, ml	128.09±30.5	140.9±35.6	135.4±32.2	0.314
LV EF, %	64.3±7.75	61.5±9.17	59.9±8.1	0.12
LA diameter, cm	4.07±0.66	4.6±0.8	5.08±0.75	0.001
LA LD, cm	6±0.7	6.9±1.2	7.4±1	0.002
LA AP, cm	3.8±0.6	4.8±0.9	5.2±1	0.001
LA TD, cm	6.11±0.9	7.3±0.9	7.07±0.9	0.003
LA vol, ml	96.9±23.6	153.9±72.05	173.7±66.05	0.001
LA area, cm^2	99.11±18.7	164.05±46.4	191.6±43.8	0.001
CFAE duration,	84.5 (78;89)	149 (112;159)	176.5 (163;196)	0.001
msec				
CFAE zones, n	3 (3;4)	6 (5;6)	8 (6;9)	0.001
CFAE surface area, cm^2	10.4 (8.7;11.9)	22.95 (19,3;24,8)	27.85 (25.9;29.9)	0.001

Intraoperative mapping

Intraoperative stage consisted of electrophysiological (EP) study, electroanatomical mapping procedure and RFA. EP findings were investigated with the help of GE CardioLab XT recording System. Mapping procedure was performed with SJM EnSite NavX (SJM EnSite Velocity, St. Jude Medical Inc., Little Canada, MN, USA). AF paroxysm was induced by the rapid atrial pacing, if patient was in sinus rhythm at the beginning of operation. This stage consisted of several steps: lead-up, CFAE mapping, fusion with CT images, post processing of endograms and CFAE calculation in cm2. After this we compared LA surface area, which have been received with the help of Knud Thomsen formula of the surface area of an ellipsoid (S≈2π[(apbp+apcp+bpcp)/3]1/p, when p » 1.6075), to total CFAE square area. All these steps were necessary to evaluate the degree of atrial remodeling.

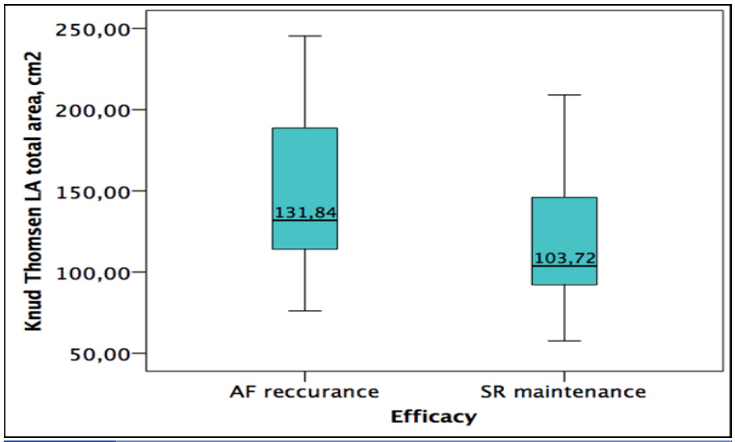

Figure 1: Median LA surface area in patients with and without sinus rhythm in 3-year follow-up

Radiofrequency ablation

Lone antral PVI was performed with open-irrigated catheters BW Celsius Thermocool (Biosense Webster, Johnson and Johnson, New Brunswick, NJ, USA) and circular diagnostic duodecapolar catheters BW Lasso. In the second type additional to PVI radiofrequency applications was performed in the areas of CFAE. The third type – endocardial "box lesion" set – consisted of antral PVI, roof line, posterior line and mitral line. After this applications CFAE areas were also ablated if they were not included in posterior box. RFA was admitted as successful if AF stopped during the procedure. Patients with AF after RFA were defibrillated.

Follow-up

Patients were discharged from the hospital on the 3d day after procedure. All of them received amiodarone for at least 6 months and warfarin for anticoagulation with target INR of 2-3. Late follow-up lasted for three years. Patients were examined after 3, 6, 12 months after ablation and then every year. AF paroxysm on ECG or Holter with duration more than 30 seconds was considered as AF recurrence.

Statistical analysis

Statistical analysis was performed with SPSS Statistics v.21 (SPSS Inc., IBM Corp. Armonk, NY, USA), statistical significance was accepted as p<0,05. Quantitative parameters that were close to the normal distribution were evaluated with median and standard deviation by the Tukey criterion. Other parameters were compared with an independent Kruskal-Wallis test for equality of medians with the help of Kendal coefficient. Regression analysis was performed with Cox test with co-variants and had an exponential graphical design. All survival curves were build with Kaplan-Meyer on the basis of evaluation of the median survival with criteria Breslow and Taron-Weyer to determine the significance of differences.

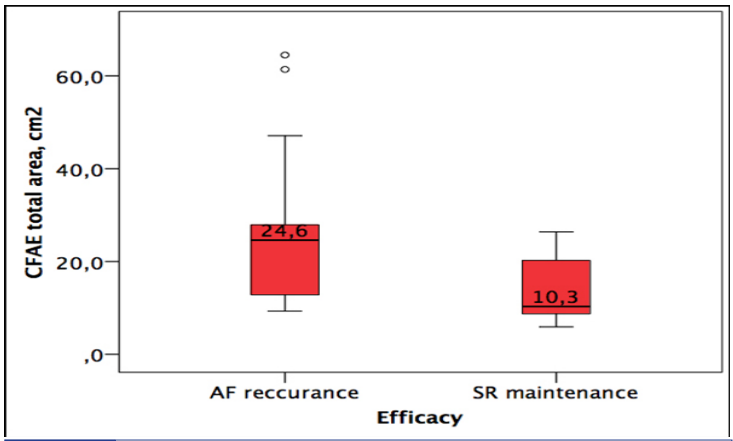

Figure 2: Median CFAE area in patients with and without sinus rhythm in 3-year follow-up

Results

The baseline characteristics of the three investigated groups are

presented in [Table 1]. There were some significant differences between the groups. First of all we are talking about LA dimensions. They varied with the deterioration of the form of AF. We noticed the enlargement of LA chamber from 96.9±23.6 ml in paroxysmal AF to 173.7±66.05 ml in LS persistent AF (p=0,001). This was rightly to LA surface area (99.11±18.7 cm^2 in paroxysmal AF to 191.6±43.8 cm^2 in LS persistent AF). Since patients with PV abnormalities were not included in the study, PV diameters didn't show meaningful diversity. For example, right and left superior PV were not much than 2.2 cm in every group. On the other hand, main parameters of LV were not significantly different (LV EF about 60-65% in all groups, p=0.12).

Prospective study

We distinguished 3 electromechanical indexes (CFAE duration, number of zones and square area) that could help us to estimate the degree of remodeling. Patients with paroxysmal AF had about 3-4 such areas with the median duration of fragmentation 84.5 msec and area 10.4 cm^2. It occupies meanly 10.5% to compare it with the total LA surface area. The same values in persistent AF were 5-6 zones, duration of 149 msec and area 22.95 cm^2, generally 13.98% of LA. In LS persistent AF 6-9 zones with duration up to 200 msec and area close to 30 cm^2, nearly 19% of LA surface.

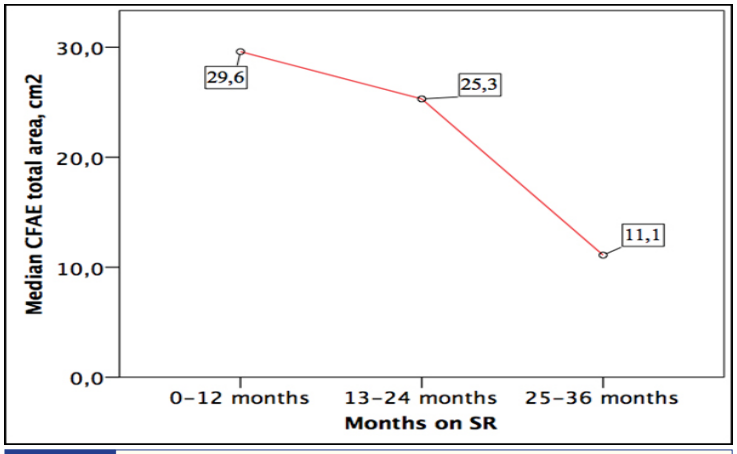

Figure 3: Relation between median CFAE total area in patients with sinus rhythm after 1, 2 and 3 years of follow-up

General efficacy of RFA was 35.8% (OR 0.3111, p 0.1644-0.5865). This value in paroxysmal group was 58.8%, in persistent 33.3% and in LS persistent 12.9% according to Kaplan-Meyer curve with p=0.001. Recurrence risk amounted 0.53, 1.09 and 2.01 in different forms of AF respectively (p=0.001). The most promising result was gained in the group of patients with paroxysmal AF, who underwent epicardial "box lesion" ablation. It was 81.8% after 3 years. The worst results were in persistent and LS persistent groups after PVI: there were no patients in sinus rhythm in 3-year follow-up with OR 0.0005, p=0.5005-0.0959 in both groups. On the whole, efficacy of different ablation techniques arised to 15.6% (OR 0.0347, p 0.0072-0.1548) in PVI 35.5% (OR 0.3030, p 0.0932-0.9643) with addition of CFAE areas and 56.3% (OR 1.6535, p 0.5502-5.0148) in "box lesion" group.

Retrospective analysis

Retrospective comparison of initial parameters showed no differences in LV parameters in patients with sinus rhythm or AF recurrence ([Table 2]). Nevertheless, all LA parameters, except diameter of right inferior PV, were extremely different. For example median LA volume in sinus rhythm patients was 102.5 ml while 25%-quartile of LA volume in another group was 114 ml. In general, all LA patterns of the sinus rhythm patients were less or equal 25%-quartile of the same patterns in patients with AF after 3-year follow-up.

Quantitative analysis of electromechanical and EP findings showed even more disappointing results. Every index in AF recurrence group was 1.5-2 times higher than its equivalent in sinus group. LA volume and surface measured by Knud Thomsen formula were 154,9ml vs 94.5ml and 131.8cm^2 vs 103.7cm^2 respectively ([Figure 1]). Median CFAE duration in AF patients was 157 msec, which is also 2 times higher (87.5msec in sinus patients). And the principal index of CFAE square area was 2.5 times bigger (24.6cm^2 vs 10.3cm^2 relatively – [Figure 2]). If we also will look at this indexes in view of every year efficacy, we will observe, that patients with less CFAE area were more likely on sinus rhythm in the end of the study ([Figure 3]).

Table 2: Initial cardiac measurements in patients with sinus rhythm and AF recurrence

Parameters	Groups	p	Median	Quartile	
				25	75
LVES, cm	AF recurrence	0,738	3,4	3,1	3,8
	SR maintenance		3,4	3,1	3,85
LVED, cm	AF recurrence	0,893	5,3	4,9	5,5
	SR maintenance		5,3	4,8	5,7
ESV, ml	AF recurrence	0,405	47,5	37,25	62,75
	SR maintenance		51	40	66
EDV, ml	AF recurrence	0,499	133,5	111,5	148,25
	SR maintenance		134	114	162
SV, ml	AF recurrence	0,457	79	68	91
	SR maintenance		82	70,5	102,75
LVEF, %	AF recurrence	0,912	62	56	66
	SR maintenance		61	56	67,5
dLA, cm	AF recurrence	0,001	4,875	4,2	5,5
	SR maintenance		4,2	3,7	4,6
LA LD, cm	AF recurrence	0,01	7	6,25	7,925
	SR maintenance		6,3	5,7	6,6
LA AP, cm	AF recurrence	0,007	4,8	4,075	5,6
	SR maintenance		4,1	3,6	4,6
LA TD, cm	AF recurrence	0,012	7,2	6,5	7,75
	SR maintenance		6,5	5,6	6,9
LA vol, ml	AF recurrence	0,0001	140	114	183,5
	SR maintenance		102,5	84,63	126,5
LA index, abs	AF recurrence	0,13	71,4	57,205	101,61
	SR maintenance		52,5	43,64	83
RSPV, cm	AF recurrence	0,013	2	1,8	2,3
	SR maintenance		1,75	1,575	2,05
RIPV, cm	AF recurrence	0,67	1,7	1,5	1,9
	SR maintenance		1,65	1,375	1,9
LSPV, cm	AF recurrence	0,04	2	1,825	2,275
	SR maintenance		1,85	1,575	2,05
LIPV,cm	AF recurrence	0,03	1,8	1,6	1,9
	SR maintenance		1,55	1,5	1,8

Discussion

We found some interesting features during our investigation, which were not observed yet in different randomized trials. First of all, we don't see systolic dysfunction even in the cases with mitral regurgitation without organic valve pathology. Anamnestic data have shown that patients suffer from moderate heart failure symptoms only on paroxysms of AF. Furthermore, they notice decrease of symptoms during the transition to persistent forms. It can be proved by EchoCG data of LV indexes, especially LV EF, that wasn't lower than 55% in all groups of patient. Contrariwise, diastolic dysfunction still is presented according to symptoms and physical analysis. We can assume that only presence of proven organic pathology of mitral valve (rheumatic disease, bacterial endocarditis, ischemic pupillary muscles dysfunction) will lead to severity of systolic heart failure in AF patient population. Recent article by Prabhu et al. can partly confirm our statement. They have shown that in patients without structural cardiomyopathy catheter ablation had resulted in improvement in symptoms and LE EF compared to patients with heart disease [4]. Close to the same results were in meta-analysis of efficacy and safety of catheter ablation vs. rate control tactics by Zhang et al [5].

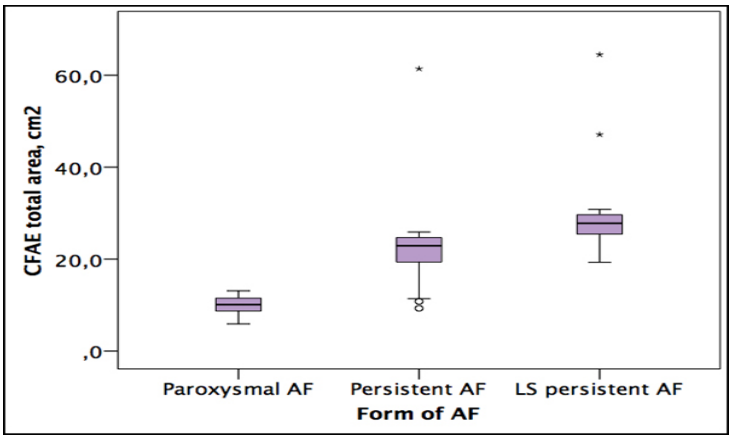

Figure 4: Median CFAE surface area in patients with different form of AF

The second thing is that there are significant differences between paroxysmal and non-paroxysmal patients, while inside the last one group they are not so expressed. It concerns all heart index values from LA volume to PV size. For example, the main parameters of our study – LA and CFAE surface areas – are twice higher in non-paroxysmal forms ([Figure 4],[Figure 5]). On the other hand, difference in persistent and LS persistent patients was not so explicit. Thus we can claim that the decisive moment of electroanatomical remodeling of atria is the transition from paroxysmal to persistent, not from persistent to LS persistent and permanent. In that case is very important to analyze and compare anamnestic data with instrumental diagnostics. [6],[7] But lack of such studies or its one-sided view leads to disclosure of one risk factor or pathologic mechanism that is responsible to one type or subtype of arrhythmia, but not for the whole process . [8] Indirectly it was verified in meta-analysis by Piccini et al, where differences among persistent and LS persistent AF were only in clinical and physiological levels, but not in diagnostically findings. [9] Hunter et al gave another interesting opinion 2010. In the CFAE AF Trial they identified that alone CFAE areas were not define the substrate of arrhythmia by themselves, but were only the expression of speed and homogeneity of AF waves, and them had changed to upwards after catheter ablation.[10]

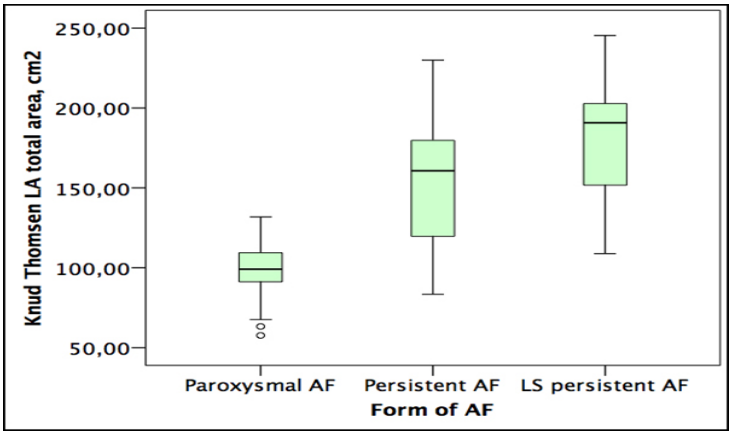

Figure 5: Median LA surface area in patients with different form of AF

Nevertheless it will be the great mistake to underestimate the role of secondary interventional procedures in maintenance of sinus rhythm in late follow-up. In our study we leaned on significance of primary catheter ablation guided by electroanatomical patterns. This is the cause of such moderate results. And it was intentionally done to separate our methods from only anatomically guided procedures. In the latter case efficacy is rather promising, and we admit the necessity of secondary ablation, as it was mentioned by Bhargava et al. in 2009 [11]. However some studies also recommend to rely on electroanatomical indexes even in the secondary procedures. [12]

Study limitations and perspectives

The study population was rather small (94 patients) and heterogeneous. We plan to enlarge it and perform the closer investigation in every type of AF patients with structural heart diseases. Also we have some doubts in validity of Holter as the main diagnostic procedure to evaluate sinus rhythm after ablation.

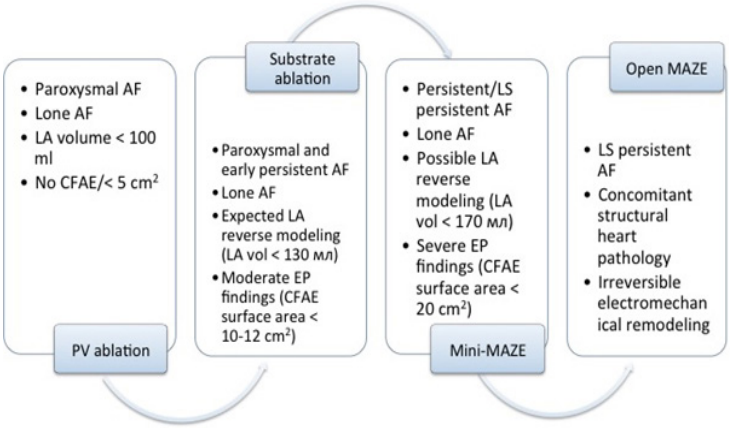

Figure 6: Stepwise approach to gain success in AF patient interventional and surgical treatment

Conclusion

Parameters of mechanical (LA volume and surface area) and electrical (CFAE duration and surface area) remodeling have to be defining in tactics and prognosis of catheter ablation in different types of AF. We recommend to apply RFA procedure in patients with LA volume less than 120ml and LA surface area less than 10-12 cm^2. At the same time electrical patterns should be the following: CFAE duration up to 150msec with surface area less than 15cm^2. In order to achieve higher efficacy we advise to use stepwise tactic

([Figure 6]).

Conflict Of Interests

None.

Disclosures

None.

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