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## THE EFFECTIVENESS OF RADIOFREQUENCY ABLATION AND REPEATED CARDIOVERSION IN COMBINATION WITH ANTIARRHYTHMIC DRUG THERAPY IN MAINTAINING STABLE SINUS RHYTHM IN PATIENTS WITH ATRIAL FIBRILLATION AND HEART FAILURE

|                             |   |
|-----------------------------|---|
| <i>Aim</i>                  | To compare the efficacy of radiofrequency ablation (RFA) and antiarrhythmic therapy (AAT) in patients with atrial fibrillation (AF) and chronic heart failure (CHF) during 12-month observation.  |
| <i>Material and methods</i> | This prospective, nonrandomized comparative observational study included 130 patients with AF (men, 65%; mean age, 62.8±11.8 years) and CHF with left ventricular ejection fraction (LV EF) <50%. Paroxysmal AF was observed in 60 (46%) patients and persistent AF was observed in 70 (54%) patients. According to results of transthoracic echocardiography (EchoCG) 107 (82%) patients had intermediate LV EF (40–49%) and 23 (18%) patients had reduced LV EF (<40%). RFA of AF was performed for 65 patients whereas 65 patients received an optimal AAT. The 24-h electrocardiogram monitoring, EchoCG, and assessment of the quality of life (QoL) with the SF-36 questionnaire were performed for all patients on admission and at 12 months of observation. Stability of sinus rhythm, EchoCG, QoL, and exercise tolerance were evaluated at 12 months of observation.       |
| <i>Results</i>              | 49 (75%) of patients in the RFA group and 26 (40%) of patients in the AAT group had stable sinus rhythm (SR) at 12 months. Repeated RFA for relapse of AF was performed for 6 (12%) of 49 patients; repeated cardioversion was performed for 16 (61.5%) of 26 patients. In the AAT group, there were more interventions for maintaining SR than in the RFA group ( $p<0.001$ ). In patients with SR of the RFA group at 12 months of observation, LV EF was increased ( $p<0.001$ ), left ventricular dimension ( $p<0.001$ ) and volume ( $p<0.001$ ) were decreased, and mental ( $p<0.001$ ) and physical ( $p<0.001$ ) components of health were improved according to the SF-36 questionnaire. In patients with SR of the AAT group, only improvement of mental ( $p<0.001$ ) and physical ( $p<0.001$ ) components of health was observed according to the SF-36 questionnaire. |
| <i>Conclusion</i>           | RFA provided a considerable decrease in the frequency of AF relapse and improvement of LV EF in patients with CHF. The effectiveness of RFA did not depend on the type of arrhythmia. For 12 months of observation, the number of hospitalizations for decompensated CHF and interventions to maintain SR decreased in the RFA group compared to the AAT group.   |
| <i>Keywords</i>             | Radiofrequency ablation; atrial fibrillation; chronic heart failure; antiarrhythmic therapy   |
| <i>For citation</i>         | Seliutskii S.I., Savina N.M., Chapurnykh A.V. The effectiveness of radiofrequency ablation and repeated cardioversion in combination with antiarrhythmic drug therapy in maintaining stable sinus rhythm in patients with atrial fibrillation and heart failure. <i>Kardiologiia</i> . 2020;60(8):90–97. [Russian: Селюцкий С.И., Савина Н.М., Чапурных А.В. Оценка эффективности радиочастотной аблации и повторной кардиоверсии в сочетании с антиаритмической терапией в поддержании устойчивого синусового ритма у пациентов с фибрилляцией предсердий и сердечной недостаточностью. <i>Кардиология</i> . 2020;60(8):90–97]   |
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The prevention and management of atrial fibrillation (AF) are among the critical issues of modern cardiology. One of the most common heart rhythm disorders, AF leads to a significant increase in the risk of thromboembolic complications, chronic heart failure (CHF), and unfavorable prognosis. The prevalence of AF in the general population is 1% – 2%; the AF incidence increased by 13% over the past 20 years [1]. The risk of AF increases with age, and is about 25% after the age of 40 [2].

Chronic heart failure is a common outcome of many cardiovascular diseases. The prevalence of CHF in various regions of the Russian Federation is 7% – 10% [3]. Despite the treatment achievements of recent decades, the prognosis for patients with CHF remains unfavorable: 5-year mortality is 50%, and 10-year mortality is 90% [4–6].

Concomitant AF and CHF are quite common, and together have a significant adverse effect on quality

of life (QoL) and prognosis. The pathophysiological background of the causality between CHF and AF has not yet been entirely determined. In AF, a decrease in cardiac output due to the loss of the contribution of atrial systole and a decrease in the time of diastolic filling of the left ventricle (LV) leads to CHF development. CHF is a powerful independent predictor of AF: the risk of AF in patients with CHF is 4.5–5.9 times higher than in patients without [7]. The prevalence of AF is proportional to the severity of CHF: from less than 5% in patients with New York Heart Association (NYHA) functional class (FC) I CHF to approximately 50% in patients with FC IV CHF [8]. The development of AF significantly affects the prognosis for patients with CHF. According to several studies, the mortality in patients with CHF and AF is significantly higher than that in patients with CHF and sinus rhythm (SR) [9, 10].

The management of patients with AF requires an individual approach to treatment. AF is managed conservatively in most cases, but drugs' efficacy may be limited in patients with long-term arrhythmia (frequent AF paroxysms, severe CHF with AF). Thus, various surgical approaches to treat AF, including radiofrequency ablation (RFA), have been developed and implemented in recent decades.

Two main methods of RFA are used in AF: RFA of the atrioventricular (AV) node with subsequent installation of a pacemaker and RFA of AF (isolation of pulmonary veins [PV], ablation of the AF focus) [11, 12]. Combined RFA is mainly used in modern clinical practice, which includes wide PV antral isolation, application of linear radiofrequency injuries in the left atrium (LA), ablation in the area of fragmented electrograms in the LA and the coronary sinus, and ablation of foci and triggers outside the LV. This tactic leads to a decrease (shutdown) of a particular area of the atrial myocardium – that is, the arrhythmia substrate. The electrophysiological outcome of this intervention is a prolongation of AF cycle and the transformation of AF into atrial flutter and/or atrial tachycardia with subsequent recovery of SR [13].

In modern interventional practice, RFA of LA anatomical structures is a common way to monitor heart rhythm in patients with AF in the case of inadequate response to drug therapy. The efficacy of RFA in maintaining SR is higher than that of conservative therapy with antiarrhythmic drugs [14]. However, the efficacy and safety of RFA in various categories of patients with AF and its effects on the immediate and long-term prognosis are not yet well known. There remain some issues of the management of patients with CHF and AF RFA. The possibilities of using AF RFA are less studied in patients with CHF of different sex and

age, with different LV ejection fraction (LVEF), and the presence of significant co-morbidities. To determine patient management and risk stratification, clear criteria of the prognostic efficacy of LV RFA in patients with AF are necessary, which is also relevant for patients with CHF.

The advantages of AF RFA over antiarrhythmic therapy (AAT) in patients with CHF have been shown mainly in small foreign studies. The efficacy of RFA, the course of CHF, and clinical outcomes in the Russian population of patients after AF RFA have not been thoroughly studied, a gap that has given rise to this study.

## Objective

To compare the efficacy of RFA and AAT in patients with paroxysmal and persistent AF and CHF during the 12-month follow-up period.

## Material and Methods

The open-label prospective observational study included 130 patients with AF and CHF with LVEF < 50% (65% male) who were admitted to the department of surgical treatment of complex heart rhythm disorders and pacing at the Central Clinical Hospital and Polyclinic of the Presidential Administration of the Russian Federation in the period of January 1, 2017 to January 31, 2019.

Inclusion criteria included paroxysmal or persistent AF, CHF with LVEF less than 50%. Exclusion criteria were ventricular arrhythmias that require antiarrhythmic therapy or RFA, paroxysmal atrioventricular reentry tachycardias, acute myocardial infarction (MI), myocarditis, pericarditis, infectious endocarditis, chronic diseases with severe organ dysfunction, malignancies, mental illnesses, alcohol abuse, and loss of contact with the patient after discharge.

The study was approved by the Ethics Committee of the Central Clinical Hospital and Polyclinic of the Presidential Administration of the Russian Federation and was performed under the Declaration of Helsinki of the World Medical Association. All patients signed an informed consent form to be included in the study.

CHF was diagnosed following the European and Russian clinical guidelines for the diagnosis and treatment of CHF [3, 15, 16]. The functional condition of hospitalized patients was evaluated using the NYHA classification of CHF. The mean age of patients was 62.8 ± 11.8 years (40–87 years). Paroxysmal and persistent AF was identified in 60 (46%) and 70 (54%) patients, respectively. According to a transthoracic echocardiogram, 107 (82%) patients had midrange LVEF (40% – 49%), and 23 (18%) patients had reduced

LVEF (< 40%). The clinical characteristics of the included patients are given in Table 1.

Patients were divided into two groups in accordance with the objective of the study: Group 1 included 65 patients hospitalized for RFA (RFA group), and Group 2 included 65 patients who received the best possible AAT due to refusal to perform RFA (AAT group). Patients were not randomized.

At inclusion and after 12 months of follow-up, all patients underwent clinical examination, including anthropometric measurements, assessment of NYHA FC, 6-minute walk test (6MWT) [17], and Short Form (SF) – 36 survey [18].

Laboratory tests were performed using a Konelab-30 system (Finland). A standard clinical blood test and serum biochemical test were conducted. The glomerular filtration rate was calculated using the CKD-EPI (chronic kidney disease epidemiology collaboration) formula.

Electrocardiogram (ECG) was recorded on EASY ECG devices (ATES MEDICA, Russia). A standard 12-lead ECG was recorded at rest. Heart rhythm, conduction disorders (degree of atrioventricular block, bundle branch block), signs of cardiac hypertrophy, ST segment, T wave, and other ECG indicators were analyzed.

24-hour Holter monitoring was performed using the BTL-08 HOLTER H600 devices (BTL, Russia). ECG was recorded in 7/12 leads. Heart rhythm, conduction disorders (degree of atrioventricular block, bundle branch block), signs of cardiac hypertrophy, ST segment, T wave, and other ECG indicators were analyzed.

Transthoracic echocardiogram was performed on a VIVID E9 device (GE Healthcare, USA). The dimensions and volumes of the heart chambers, the ventricular septum's thickness in diastole, and the posterior wall thickness of the LV were determined. LVEF (%) was assessed by Simpson's biplane method.

Transesophageal echocardiography was used to assess the left atrial appendage (LAA) ejection rate to identify LAA abnormalities.

The chest X-ray examination was carried out to detect venous congestion, pleural effusion, infiltrative changes, and increased size of the chambers of the heart and blood vessels.

The duration of follow-up after discharge was 12 months. The following events were reported: total mortality, cardiovascular death, acute MI, stroke, a progression of CHF, relapses of AF, repeated interventions, and SR stability. Echocardiogram, SF-36 survey, and 6MWT were performed 1, 3, 6, and 12 months after inclusion.

Statistical processing of the study results was performed using the standard SPSS 25.0 software suite. The

**Table 1.** Clinical characteristics of the included patients (n=130)

| Parameter  | Number of patients | %   |
|--|--------------------|-----|
| Male   | 84                 | 65  |
| Female   | 46                 | 35  |
| Cardiovascular and concomitant pathology           |                    |     |
| CAD (including a history of myocardial infarction) | 73                 | 56  |
| History of myocardial infarction                   | 33                 | 25  |
| History of coronary artery bypass grafting         | 11                 | 8   |
| Hypertension                                       | 127                | 98  |
| Valvular heart disease                             | 10                 | 8   |
| Left ventricular aneurysm                          | 10                 | 8   |
| Paroxysmal AF                                      | 60                 | 46  |
| Persistent AF                                      | 70                 | 54  |
| History of ventricular fibrillation                | 2                  | 1.5 |
| Type 2 diabetes                                    | 29                 | 22  |
| History of CVA/TIA                                 | 9                  | 7   |
| History of PE                                      | 3                  | 2   |
| CKD  | 10                 | 8   |
| Obesity  | 16                 | 12  |
| FC II–III  | 71                 | 54  |
| LVEF 40%–49%                                       | 107                | 82  |
| LVEF <40%  | 23                 | 18  |

The data are expressed as the absolute and relative rates, n (%). CAD, coronary artery disease; AF, atrial fibrillation; CVA/TIA, cerebrovascular accident/transient ischemic attack; PE, pulmonary embolism; CKD, chronic kidney disease; FC, functional class; LVEF, left ventricular ejection fraction.

distribution of variables was estimated using the Kolmogorov–Smirnov test. As the distribution of quantitative variables was normal, the mean (M) and the standard deviation (SD) were calculated. The categorical signs are expressed as the absolute (n) and relative (%) values. Pearson's  $\chi^2$  test was used to compare the rates. The mean values were compared using the univariate analysis of variance (ANOVA) and Fisher's exact test. The differences were statistically significant at  $p < 0.05$ .

## Results

Table 2 shows a comparison of the clinical characteristics of patients in the groups studied. The groups are comparable in the ratio of patients with paroxysmal and persistent AF, LVEF, and co-morbidities.

There were no significant differences in echocardiogram, 6MWT, and QoL between the groups studied at the time of inclusion.

In the RFA group, the pulmonary veins were isolated in all patients; focal ablation and application of linear lesions were performed, if necessary.

Table 3 shows the comparative characteristics of drug therapies in patients in the groups analyzed. All patients in the groups studied took anticoagulants.

There were differences in the rates of prescribing class 1C antiarrhythmic drugs between the RFA and AAT groups (34% and 8%, respectively;  $p<0.001$ ).

### Results of the 12 month follow-up of patients with AF and CHF

The 12-month SR stability (according to the 24-hour Holter monitoring at 1, 3, 6, 12 months) was 75% ( $n=49$ ) in the RFA group and 40% ( $n=26$ ) in the AAT group ( $p<0.001$ ). Repeated RFA procedures for recurrent AF were carried out in 6 of 49 (12%) patients. Repeated cardioversions were performed for 16 of 26 (61.5%) patients in the AAT group. There were more interventions to preserve SR in the AAT group than in the RFA group ( $p<0.001$ ), as well as more hospitalizations due to decompensated CHF [39 (60%) in the AAT group, 15 (23%) in the RFA group;  $p<0.001$ ].

Table 4 shows changes in echocardiogram, 6MWT, and SF-36 at 12 months after AF RFA in the RFA group and the 12-month changes in the same scores in the AAT group. It also shows comparative characteristics of echocardiogram, 6MWT, and QoL in the RFA and AAT groups after 12 months of follow-up.

Patients in the RFA group showed an increase in LVEF ( $p<0.001$ ) and LV end-diastolic dimension (LVEDD) ( $p<0.001$ ), a decrease in the LA dimension ( $p<0.001$ ) and volume ( $p<0.001$ ), an improvement in 6MWT ( $p=0.006$ ), and an improvement in the mental ( $p<0.001$ ) and physical ( $p<0.001$ ) health SF-36 components after 12 months of follow-up. Patients in the AAT group only showed the improvement in the mental ( $p<0.001$ ) and physical ( $p<0.001$ ) health SF-36 components. There were no statistically significant differences in patients with paroxysmal and persistent arrhythmia in any of the groups.

After 12 months of follow-up, there were statistically significant differences in LVEF ( $p<0.001$ ), LA volume ( $p=0.035$ ), 6MWT ( $p<0.001$ ), and mental and physical health ( $p=0.038$  and  $p=0.047$ , respectively).

Table 5 presents the characteristics of drug therapies in the groups studied after the 12-month follow-up.

After 12 months of follow-up, significant differences were found in the rates of administration of beta-blockers ( $p=0.002$ ) and anticoagulants ( $p<0.001$ ).

AAT was prescribed based on 24-hour Holter monitoring (registration of atrial tachycardias, unstable paroxysms of AF) in the RFA group. The hospital's cardiologists and arrhythmologists agreed on the administration of AAT.

**Table 2. Clinical profiles of the patients by study groups**

| Parameter   | RFA group (n=65) | AAT group (n=65) | p*    |
|---|------------------|------------------|-------|
| Age, years  | 63.7+8.9         | 61.4+11.3        | 0.625 |
| Cardiovascular and concomitant pathology                  |                  |                  |       |
| CAD (including a history of myocardial infarction), n (%) | 39 (60)          | 34 (52)          | 0.704 |
| History of myocardial infarction, n (%)                   | 18 (28)          | 15 (23)          | 0.546 |
| History of coronary artery bypass grafting, n (%)         | 7 (11)           | 4 (6)            | 0.345 |
| Hypertension, n (%)                                       | 63 (97)          | 64 (98)          | 0.560 |
| Valvular heart disease, n (%)                             | 4 (6)            | 6 (9)            | 0.511 |
| Left ventricular aneurysm, n (%)                          | 4 (6)            | 6 (9)            | 0.511 |
| Paroxysmal AF, n (%)                                      | 29 (45)          | 31 (48)          | 0.725 |
| Persistent AF, n (%)                                      | 36 (55)          | 34 (52)          | 0.725 |
| History of ventricular fibrillation, n (%)                | 2 (3)            | 0 (0)            | -     |
| Type 2 diabetes, n (%)                                    | 11 (17)          | 18 (28)          | 0.141 |
| History of CVA/TIA, n (%)                                 | 3 (5)            | 6 (9)            | 0.300 |
| PE, n (%)   | 2 (3)            | 1 (2)            | 0.560 |
| CKD, n (%)  | 4 (6)            | 6 (9)            | 0.511 |
| Obesity, n (%)  | 9 (14)           | 7 (11)           | 0.594 |
| CHF FC II–III, n (%)                                      | 34 (52)          | 37 (57)          | 0.856 |
| LVEF 40%–49%, n (%)                                       | 54 (83)          | 53 (82)          | 0.819 |
| LVEF<40%, n (%)   | 11 (17)          | 12 (18)          | 0.819 |

The data are expressed as the absolute and relative rates, n (%); \*,  $\chi^2$  or Fisher exact test and univariate analysis of variance were used.

RFA, radiofrequency ablation; AAT, antiarrhythmic therapy; CAD, coronary artery disease; AF, atrial fibrillation; CVA/TIA, cerebrovascular accident/transient ischemic attack; PE, pulmonary embolism; CKD, chronic kidney disease; FC, functional class; LVEF, left ventricular ejection fraction.



**Table 3. Pre-hospital drug therapy**

| Parameter                                     | RFA group (n=65) | AAT group (n=65) | p*      |
|---|------------------|------------------|---------|
| ACE inhibitors, n (%)                         | 48 (74)          | 45 (69)          | 0.560   |
| Beta-blockers, n (%)                          | 52 (80)          | 55 (85)          | 0.475   |
| Mineralocorticoid receptor antagonists, n (%) | 8 (12)           | 12 (18)          | 0.331   |
| Anticoagulants, n (%)                         | 65 (100)         | 65 (100)         | -       |
| Warfarin, n (%)                               | 8 (12)           | 12 (18)          | 0.331   |
| Rivaroxaban, n (%)                            | 40 (61.5)        | 32 (49)          | 0.159   |
| Dabigatran, n (%)                             | 10 (15)          | 14 (21.5)        | 0.366   |
| Apixaban, n (%)                               | 6 (9.5)          | 7 (11)           | 0.771   |
| NOACs, total, n (%)                           | 56 (86)          | 53 (81.5)        | 0.475   |
| Heparin, n (%)                                | 1 (1.5)          | 0 (0)            | -       |
| Calcium antagonists, n (%)                    | 15 (23)          | 19 (29)          | 0.425   |
| Statins, n (%)                                | 47 (72)          | 52 (80)          | 0.304   |
| Antiarrhythmic drugs, class IC (%)            | 22 (34)          | 5 (8)            | < 0.001 |
| Amiodarone, n (%)                             | 13 (20)          | 10 (15)          | 0.491   |

The data are expressed as the absolute and relative rates, n (%); \*,  $\chi^2$  or Fisher exact test was used. RFA, radiofrequency ablation; AAT, antiarrhythmic therapy; ACE, angiotensin-converting enzyme; NOACs, new oral anticoagulants.

**Table 4. Changes in echocardiogram, 6 minute walk test, and quality of life in the patient groups during 12-month follow-up**

| Parameter                         | RFA group, n=65 |                     |         | AAT group, n=65 |              |         | Differences between groups after 12 months of follow-up, p* |
|-----------------------------------|-----------------|---------------------|---------|-----------------|--------------|---------|---|
|                                   | Before RFA      | 12 months after RFA | p*      | At inclusion    | In 12 months | p*      |   |
| LVEF, %                           | 43.63±2.76      | 49.48±7.20          | < 0.001 | 43.19±3.22      | 42.71±3.54   | 0.808   | <0.001  |
| LA dimension, mm                  | 45.6±4.4        | 43.4±4.1            | < 0.001 | 45.1±4.5        | 44.1±4.6     | 0.321   | 0.295   |
| LA volume, mL                     | 96.08±19.30     | 85.00±16.22         | < 0.001 | 92.65±17.75     | 95.65±15.61  | 0.649   | 0.035   |
| LVEDD, mm                         | 55.0±7.9        | 52.4±6.9            | < 0.001 | 55.6±7.2        | 56.6±7.2     | 0.171   | 0.459   |
| Mental health component, score*   | 38.39±2.58      | 47.23±5.54          | < 0.001 | 37.79±3.16      | 45.28±9.23   | < 0.001 | 0.038   |
| Physical health component, score* | 42.50±6.23      | 49.47±9.42          | < 0.001 | 39.41±4.46      | 48.96±7.85   | < 0.001 | 0.047   |
| 6 minute walk test, m             | 321.43±75.36    | 371.83±82.92        | 0.006   | 302.0±92.78     | 332.0±76.9   | 0.205   | < 0.001   |

Data are expressed as the mean and standard deviation (M±SD); \*, univariate analysis of variance was used.

RFA, radiofrequency ablation; AAT, antiarrhythmic therapy; LVEF, left ventricular ejection fraction;

LA, left atrium; LVEDD, left ventricular end diastolic dimension; \*, SF-36 was used.

No statistically significant differences were found for other groups of drugs.

The 12-month mortality rate was 1.5% (1 patient in the RFA group; the cause of death was intestinal obstruction). No deaths were registered in the AAT group.

There were 3 (4.6%) and 5 (7.7%) cases of MI in the RFA and AAT groups, respectively, in the 12 month follow-up period. Cerebrovascular accident (CVA) was detected in 4 (6%) and 7 (11%) patients in the RFA and AAT groups, respectively.

## Limitations

At baseline, the RFA and AAT groups were not initially comparable in any parameters, as patients were not randomized at enrollment. Significant differences

were revealed in the administration of antiarrhythmic drugs class IC at the time of inclusion (34% in the RFA group and 8% in the AAT group;  $p < 0.001$ ).

## Discussion

According to our findings, AF RFA has significant advantages over conservative therapy in maintaining stable SR in patients with CHF and reduced/midrange LVEF. Patients showed improvements in the LV contractility, and dimensions of the left heart chambers reduced after RFA. Also, a decrease in the LA dimensions may result from radiofrequency exposure (areas of connective tissue compressing the cavity are formed after the application of lesions). Exercise tolerance improved according to 6MWT, as well as physical and mental health, according to the SF-36 questionnaire.

**Table 5.** Drug therapies used in the groups studied after 12 months of follow-up

| Parameter                                     | RFA group (n=65) | AAT group (n=65) | p*      |
|---|------------------|------------------|---------|
| ACE inhibitors, n (%)                         | 48 (74)          | 45 (69)          | 0.560   |
| Beta-blockers, n (%)                          | 41 (63)          | 57 (88)          | 0.002   |
| Mineralocorticoid receptor antagonists, n (%) | 8 (12)           | 12 (18)          | 0.331   |
| Anticoagulants, n (%)                         | 55 (85)          | 65 (100)         | < 0.001 |
| Warfarin, n (%)                               | 8 (12)           | 12 (18)          | 0.331   |
| Rivaroxaban, n (%)                            | 33 (51)          | 32 (49)          | 0.861   |
| Dabigatran, n (%)                             | 10 (15)          | 14 (21.5)        | 0.366   |
| Apixaban, n (%)                               | 4 (7)            | 7 (11)           | 0.345   |
| NOACs, total, n (%)                           | 47 (73)          | 53 (81.5)        | 0.212   |
| Calcium antagonists, n (%)                    | 15 (23)          | 19 (29)          | 0.425   |
| Statins, n (%)                                | 47 (72)          | 52 (80)          | 0.304   |
| Antiarrhythmic drugs, class 1C (%)            | 14 (21.5)        | 9 (14)           | 0.251   |
| Amiodarone, n (%)                             | 7 (11)           | 12 (18)          | 0.215   |

Data are expressed as the absolute and relative rates, n (%); \*,  $\chi^2$  or Fisher exact test was used. RFA, radiofrequency ablation; AAT, antiarrhythmic therapy; ACE, angiotensin-converting enzyme; NOACs, new oral anticoagulants.

Moreover, there was a significant decrease in the rates of administration of beta-blockers and anticoagulants in the RFA group, which is associated with better efficacy of RFA in maintaining stable SR and less frequent recurrences of arrhythmia.

Thus, RFA is suitable as the method of choice in treatment of patients with AF and CHF. The advantages of RFA over conservative therapy are apparent. For example, AF RFA and standard drug therapy for AF in patients with CHF with reduced LVEF were compared in the recent CASTLE-AF trial [19]. This prospective randomized clinical trial (RCT) included 363 patients from the United States, Europe, Australia, and South Africa. The inclusion criteria were age over 18 years; symptomatic paroxysmal or persistent AF; no effect from amiodarone or refusal of the patient to take it; LVEF<35%, NYHA FC II–IV; implanted cardioverter defibrillator with automatic remote monitoring. The RFA group consisted of 179 patients, and the AAT group included 184 patients. The mean follow-up period was 37.8 months.

The primary endpoint was all-cause death or deterioration of CHF, which required hospitalization. The main secondary endpoints were all-cause death, CHF progression requiring hospitalization, cardiovascular death, stroke, hospitalization for cardiovascular and other diseases. The RFA group also evaluated the postsurgery complications and the duration of SR stability. The primary endpoint was achieved in a smaller number of cases in the RFA group compared with the AAT group (28.5% vs. 44.6%; odds ratio [OR] 0.62, 95% confidence interval [CI]: 0.43–0.87;  $p=0.007$ ). The secondary endpoints were also recorded less frequently

in the RFA group: all-cause death 13.4% versus 25% (OR 0.53, 95% CI: 0.32–0.86;  $p=0.011$ ), hospitalization for deterioration of CHF 20.7% versus 35.9% (OR 0.56, 95% CI: 0.37–0.83;  $p=0.004$ ), cardiovascular death 11.2% versus 22.3% (OR 0.49; 95% CI: 0.29–0.84;  $p=0.009$ ). According to the data stored in the implanted devices, SR was preserved for 6 months of the follow-up in 63.1% of patients in the RFA group and 21.7% in the AAT group ( $p<0.001$ ). In addition, RFA led to an increase in the 6MWT distance and LVEF, according to echocardiogram [19]. Thus, this is the first RCT that showed a significant advantage of AF RFA in patients with CHF with reduced LVEF in a relatively large sample.

Anselmino et al. (2014) also demonstrated the efficacy of RFA in a systematic review and meta-analysis of 26 RCTs, including 1,838 patients with LV systolic dysfunction who were subjected to AF RFA [20]. The mean follow-up period was 23 months. SR was stable in 60% of patients by the end of the follow-up period. Analysis of the trials found that the rate of recurrent AF was significantly lower in the absence of structural heart disease ( $p=0.003$ ). During the follow-up period, we observed a significant mean increase in LVEF by 13% ( $p<0.001$ ). There were also significantly fewer patients with LVEF of less than 35% ( $p<0.001$ ). The levels of N-terminal pro-brain natriuretic peptide (NT-proBNP), which were also assessed in these trials, decreased by a mean of 620 pg/mL ( $p<0.001$ ). According to the findings, the efficacy of AF RFA in patients with left ventricular systolic dysfunction is much higher if surgery is performed soon after AF and CHF detection. It was shown that LV function gradually improves over 1–2 years, while the number of patients with severe LV

systolic dysfunction significantly decreases [20]. This review significantly enriched and strengthened the evidence base for the use of RFA in patients with AF and CHF with reduced LVEF.

There are significantly fewer data on the use of RFA in patients with AF and CHF in the Russian clinical practice. Ardashev et al. performed a 5-year observational study [21] to compare the RFA results in patients with long-lasting persistent AF (rhythm control) and drug therapy aimed at controlling heart rate. The study included 132 patients with AF. The RFA group consisted of 66 patients (58 male, mean age  $53.3 \pm 12.3$  years) with long-lasting persistent AF. The control group of patients was comparable with the RFA group in sex, age, and duration of arrhythmia history. It included 66 patients with persistent AF (56 male, mean age  $54.2 \pm 11.6$  years) who received medication. All patients included had CHF of varying clinical severity: 14 patients in the RFA group and 11 patients in the control group had NYHA FC III–IV.

No recurrent AF and atrial tachyarrhythmia were observed in 49 (74%) patients in the first 12 months of follow-up after the initial intervention. SR remained stable in 38 of 42 (56%) patients in the RFA group who remained under supervision for 5 years, 21 (32%) of whom did not receive AAT. The absence of the RFA effect was observed only in 4 (6%) patients, and AF preserved in all cases in the control group. After 5 years of follow-up, there were no cases of myocardial or ischemic stroke in the RFA group ( $n=42$ ), while there were 5 cases of MI ( $p=0.006$ ) and 6 cases of stroke ( $p=0.001$ ) in the control group. FC improved in 23 (35%) patients in the RFA group and only 2 (3%) patients in the control group ( $p=0.002$ ). Moreover, 17 (26%) patients in the control group had long-lasting AF and concomitant

deterioration of CHF FC. CHF progressed (according to the rate of hospitalizations, echocardiogram, and NYHA FC) in 6% and 25% of patients in the RFA group and the control group, respectively ( $p=0.006$ ).

The authors concluded that RFA provides high treatment efficacy despite a long-lasting arrhythmic history. Stable SR in these patients is associated with a significant reduction in the incidence of cardiovascular complications and the clinical severity of CHF [21].

The results of a few Russian studies, including those obtained in our study, are generally comparable to the results of foreign randomized and observational studies, and significantly expand the possibilities of using RFA in clinical practice. However, the evidence obtained to date does not allow us to fully assess the significance of RFA techniques in the treatment of paroxysmal and persistent AF in patients with different LVEF and clinical severity of CHF or to draw convincing conclusions about the effect of AF RFA on the long-term prognosis for patients with CHF and different LVEF.

## Conclusion

Radiofrequency ablation significantly reduces the incidence of recurrent atrial fibrillation and improves echocardiographic performance in patients with chronic heart failure and midrange/reduced LVEF. During the 12-month follow-up period, hospitalizations for decompensated chronic heart failure and interventions to preserve sinus rhythm decreased in the group of radiofrequency ablation, unlike the antiarrhythmic therapy group.

*No conflict of interest is reported.*

**The article was received on 31/10/2019**

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