Long-Term Results of Catheter Ablation in Patients with Drug Refractory Atrial Fibrillation

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Summary

The aim of this study was to investigate the efficacy of using radiofrequency ablation of the atrioventricular junction followed by pacemaker implantation for the treatment of highly symptomatic permanent tachy-systolic atrial fibrillation. From November 1997 to April 2000, we performed radiofrequency ablation on 105 patients. The method included the conventional right-sided approach of the His bundle using a two-electrode technique. We used a variety of tools to analyze the outcome and effectiveness of these methods including: a patient quality of life questionnaire (Medical Outcomes Study Short-Form Health Survey; SF-36), a local specific questionnaire (SQ-10), and use of medications (both quantitatively and qualitatively) to determine the level of improved health and ability to work. Follow-ups were repeated at 3, 6, 12, 18, and 24 months following the procedures; the quality of life questionnaires were administered every 6 months. The number of postoperative hospitalizations and doctor visits were also tracked. Our analyses showed that radiofrequency ablation of the atrioventricular junction, followed by implantation of a DDDR or a VVIR pacemaker are effective methods of stabilizing the heart rhythm of patients suffering from chronic, drug refractory paroxysmal and permanent tachy-systolic atrial fibrillation, particularly following mitral valve replacement.

Key Words

Radiofrequency catheter ablation (RFA), atrial fibrillation (AF)

Introduction

Atrial rhythm disturbances are one of the most serious problems currently treated in cardiology and cardiac surgery practices (Table 1) [1]. In developed countries, the epidemiology of atrial arrhythmias, primarily atrial fibrillation (AF), has increased in both intensity and incidence. It also significantly influences a person's quality of life and life expectancy [2-6]. The prevalence of AF in the world varies from 1.6% – 2%; it is primarily observed in patients suffering from other cardiovascular diseases. In persons over the age of 65, AF is seen 9.1 times more frequently than in younger patients [5]. Even if radiofrequency catheter ablation (RFA) is used to treat only tachy-systolic AF patients who are resistant to drug therapy [7], the number of potential RFA candidates remains very high. According to Brignole et al. [8], the number of RFA candidates in Europe could reach a total of 396,000 (Table 2), from which 216,000 are over 65 years old [5]. Atrial fibrillation also causes a significant burden to the health care system. Complications related to AF are summarized in Tables 3 and 4, according to the Framingham study and ALFA study, respectively [9-12]. The risk of complications as well as the increasing age of the Europeans requires more active and radical intervention methods in patients with AF and ineffective drug treatment. Postoperative arrhythmias, paroxysmal AF, and atrial flutter often cause complications in relatively stable patients during a normally unevent-

Arrhythmia category	No. of patients (%)
Arrest	13,926 (2.7)
Ventricular fibrillation	8,529 (1.6)
Ventricular tachycardia	52,013 (9.6)
Supraventricular tachycardia	
Atrial fibrillation	179,018 (34.6)
Atrial flutter	23,420 (4.5)
Paroxysmal atrial tachycardia or Wolff-Parkinson-White Syndrome	30,011 (5.8)
Premature beats	30,533 (6.0)
Sick sinus	44,943 (8.7)
Conduction abnormality	43,368 (8.4)
Unspecified	91,938 (17.8)

Table 1. Distribution of hospital discharges with arrhythmia as principal diagnosis [1]. Atrial fibrillation accounts for 1/3 of all discharges.

No. of inhabitants in 35 European countries	513,000,000
People with AF	8,200,000 (1.6% of inhabitants)
Paroxysmal form of AF	3,300,000 (40% of AF)
Drug refractory AF	396,000 (12% of paraxysmal AF)

Table 2. The prevalence of atrial fibrillation in Europe [8].

Mortality	Cases	Control	Risk ratio
Total	29 (59.2%)*	84 (34.3%)	1.7
Cardiavasculary	21 (42.9%)*	52 (21.2%)	2.0

*Table 3. Mortality of patients developing atrial fibrillation during a 22-year follow-up in the Framingham study [9]. * = p-value < 0.05.*

Palpitation	54.1%
Chest pain	10.1%
Dyspnea	44.4%
Syncope, dizzy spells	10.4%
Fatigue	14.3%
Other	0.9%
None	11.4%

Table 4. Prevalence of symptoms caused by atrial fibrillation in 756 patients participating in the ALFA study [12].

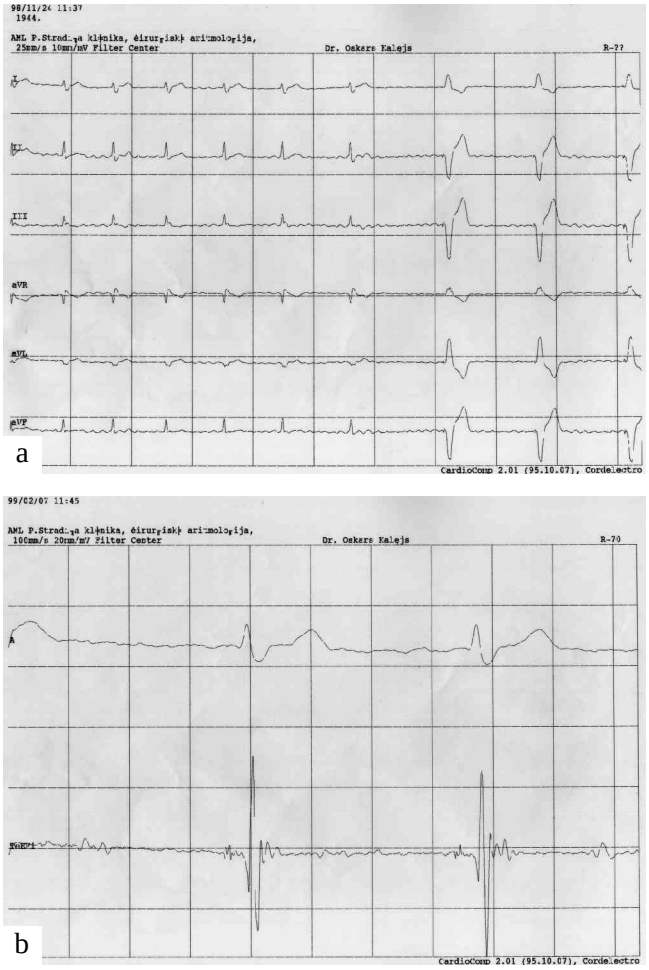


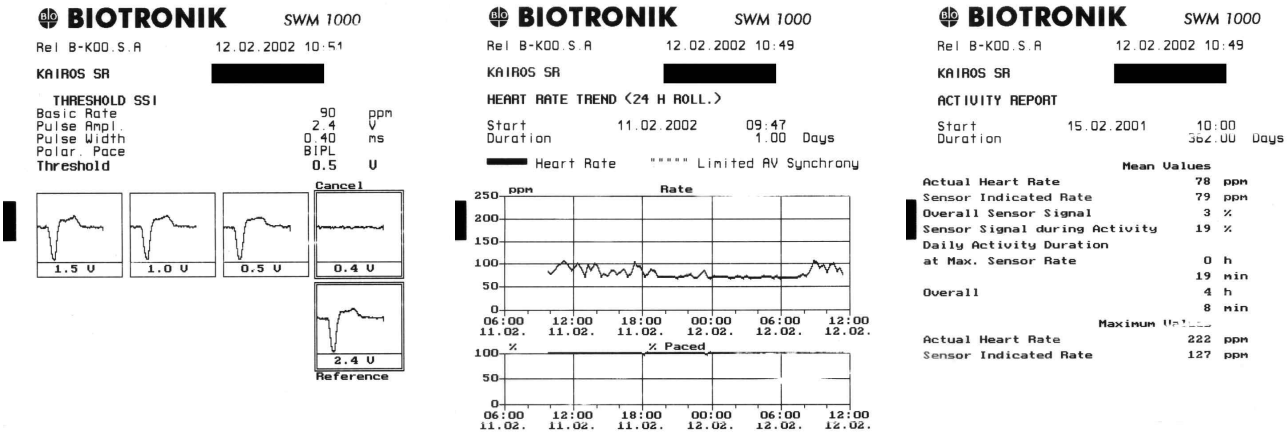
Figure1. Surface ECG during a radiofrequency ablation procedure, showing a decreasing heart rate followed by permanent pacing (a). Recordings made 3 months later: ECG and His-bundle electrogram (b).

ful postoperative period. This increases both their hospitalization time and postoperative costs [2,3,5,7, 13,14]. The situation in Latvia is shown in Table 5.

The first catheter ablation of the atrioventricular (AV) junction in patients with supraventricular arrhythmia was performed in the U.S. in 1982 by Sheinman et al. [14] and Gallagher et al. [15]. A pacemaker was then implanted to provide adequate regularity of ventricular contractions. The RFA technique became part of standard practice in 1986 after studies were performed by Huang et al. [16]. These methods resulted in total AV block, which made the patient pacemaker-dependent. Another method known as AV junction (AVJ) modulation, developed later on, used a varied amount of energy and interrupted supply. The modulation reduced the

Type of arrhythmia	Total calls	No. of emergency visits	Hospitalized	Total costs (Latvian lats)
Paroxysmal supraventricular tachycardia; AVNRT, WPW, Ect. SVT	1530	1497	1233	48,519
Paroxysmal atrial flutter	229	208	201	42,069
Atrial fibrillation	3691	3557	2134	108,800
Paroxysmal ventricular tachycardia	59	56	53	11,100
2nd and 3rd degree AV block	181	152	152	33,874
Other arrhythmias	693	647	446	72,918
Total	6383	6117	4219	317,279

Table 5. Different types of heart rhythm disturbances leading to emergency room visits in Riga, Latvia, 2000. 1 Latvian lats = 1.78 Euro.



a b c

Figure 2. Example of a pacemaker follow-up: threshold analysis (a), intracardiac ECG and pacemaker diagnostics (b), pacemaker programming and surface ECG (c). See text for additional information on the patient.

amount of impulses transmitted from the atria to the ventricles, which causes ventricular contractions. The undisputed advantage of the latter method is the patient's independence from the implanted pacemaker, unless total AV block develops.

Radiofrequency ablation is most frequently performed at the posteriorseptal area near the coronary sinus, where the His potential is not registered any more and The ratio between atrial and ventricular sensed amplitudes is < 1. The RFA is applied during 45 – 90 s, using the power of 30 – 35W [3,17,18]. Several studies have shown that RFA of the AVJ followed by pacemaker implantation effectively treats patients with drug refractory AF [2,3,5,7,8,13,18,19]. The analogy of clinical results for patients with paroxysmal AF and patients with chronic AF is uncertain [5,18,20,21]. Theoretically, patients with paroxysmal AF should experience a greater degree of negative effects due to the procedure, because RFA may eliminate atrial synchronization (which will then impede the atria's ability to fill the ventricles). Conversely, patients with chronic AF already have poorly functioning atria as a result of the disease, so that the negative influence of RFA manifests only with an asynchronous contraction of the ventricles.

In Latvia, catheter ablation of the AVJ following pacemaker implantation is one of the primary treatments for chronic tachy-systolic, drug refractory AF. Many of these patients also undergo mitral valve replacement (MVR). The purpose of our study was to analyze the results of patients with chronic, uninterrupted AF and permanent drug refractory tachy-systolic AF who were treated with RFA (Group A in Table 6). From November 1997 to April 2000, RFA was performed on 105 patients. This group was compared to the control

	Permanent AF		Paroxysmal AF		p-value
	Group A	Group B	Group A	Group B	
No. of patients	70	77	35	41	
Mean age ± SD (years)	64 ± 23	63 ± 18	59 ± 18	60 ± 15	0.1
Sex (% female)	55	58	49	54	
LV grade (%)					
EF > 60%	15	16	21	22	
EF = 40 – 59%	74	80	71	70	
EF = 21 – 39%)	11	4	8	8	0.09
NYHA functional class (%)					
I	0	0	2	1	
II	25	31	35	38	
III	68	66	58	60	
IV	7	3	5	1	0.05
Paroxysm duration (%)					
< 1 year			6	6	
1 – 3 years			60	61	
> 3 years			34	33	0.05
AF duration (%)					
< 3 months	16		18		
3 – 12 months	40		39		
> 12 months	44		43		0.05
Left atrial size (%)					
< 40 mm	6	7	2	2	
40 – 50 mm	18	19	32	34	
51 – 60 mm	54	53	55	55	
> 60 mm	22	23	11	9	0.001
History of stroke (%)	8	10	1	1	
Mitral valve lesion (%)					
Stenosis	0	2	6	7	
Regurgitation	72	68	70	74	
Mixed	28	30	24	19	
Previously performed mitral valve replacement	24 (34%)	18 (23%)	6 (17%)	10 (24%)	
Coronary artery disease, previously revascularised	11 (15%)	14 (18%)	3 (8.5%)	7 (17%)	
Evidential bradiarrhythmias	18 (25%)	2 (4%)	10 (28%)	1 (2%)	

Table 6. Patient characteristics for groups A and B. Paroxysm duration is given for patients with paroxysmal atrial fibrillation (AF) and AF duration for patients with permanent AF. Since February 2000, the preferred method of treatment has been pulmonary vein isolation with concomitant valve replacement.

group (Group B in Table 6) that received drug treatment without RFA following pacemaker implantation. In some patients of Group A, the MVR was also performed from 1986 to 1999 [22]. The shortest period between MVR and RFA treatment was 60 days, the longest period was 12 years. Prior to enrollment in the study the patients were informed about the study purpose, methods, and methodological differences; patients were allowed to withdraw from the study at any point and choose another treatment.

Materials and Methods

The inclusion criteria for Group A (RFA) were:

- Chronic, uninterrupted drug refractory AF;
- Stable, permanent, drug refractory tachy-systolic AF;
- Increasing NYHA class or ineffective drug treatment;
- Left ventricular function disorder; i.e., ejection fraction (EF) < 45%;
- Increased amount of drugs without a significant positive effect;
- Intolerance to some drug groups, intolerance to increased doses.

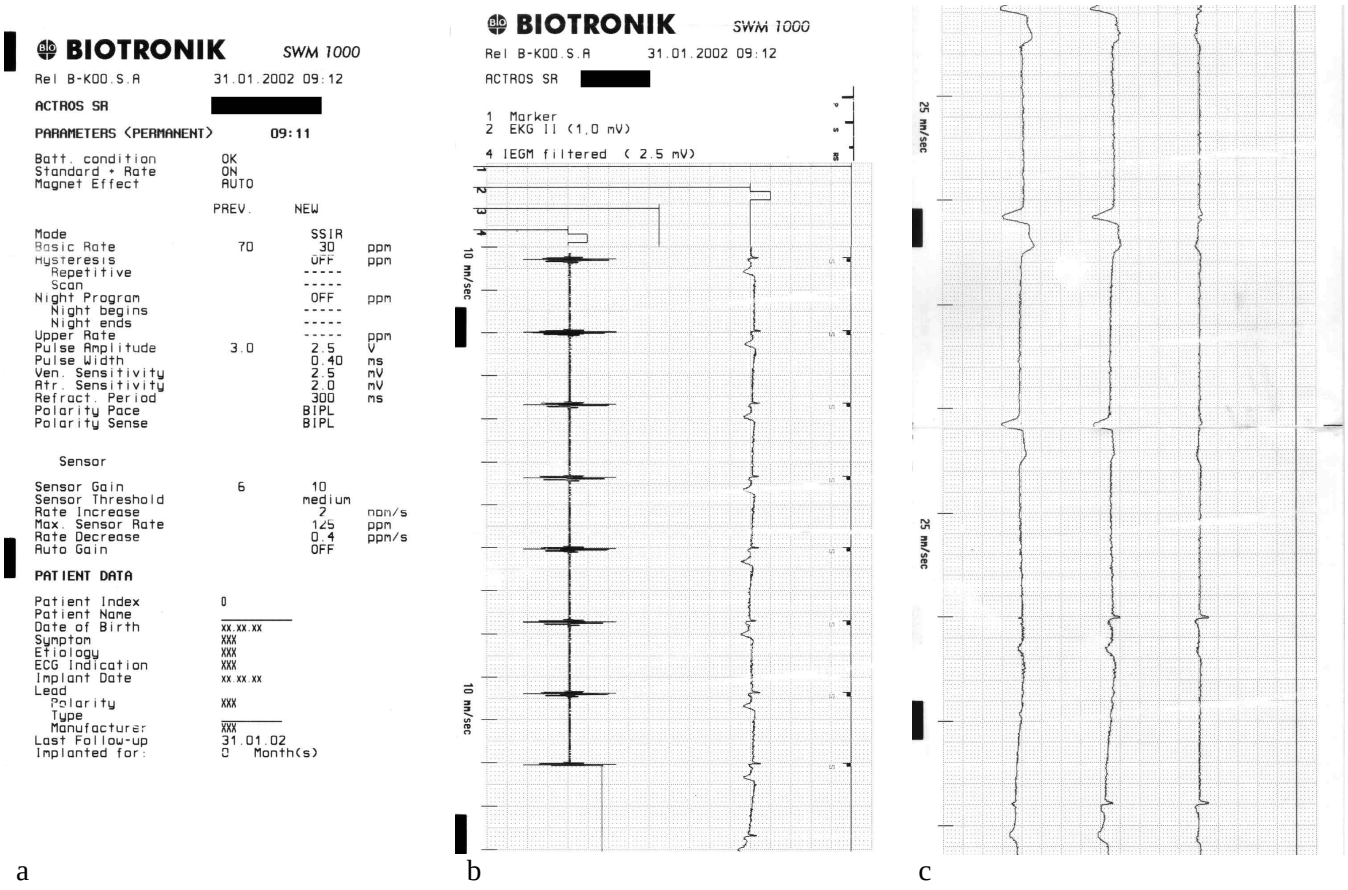


Figure 3. Example of a pacemaker follow-up: programmed parameters (a), intracardiac ECG (b), surface ECG (c).

For Group B (drug treatment), the period of anamnesis (in Group A it was the period following MVR) was the same as for Group A, with the longest period of 12 years. The differences in gender and age between the two groups were insignificant. The inclusion criteria for Group B were:

- Chronic, uninterrupted drug refractory AF;
- Stable, permanent, drug refractory tachy-systolic AF;
- Increasing NYHA class or ineffective drug treatment;
- Left ventricular function disorder; i.e., ejection fraction (EF) < 45%;
- Increased amount of drugs without a significant positive response;
- Intolerance to some drug groups, intolerance to increased doses;
- Patient refusal of RFA.

The procedure included a conventional right-sided RFA approach to the His bundle (AbControl/A, Biotronik, Germany), using a two-electrode approach (AlCath, Biotronik; 4-mm-tip lead, Daig, USA). It was often difficult to localize the application area. The mean X-ray time usually varied from 12 to 28 min, the maximum was 42 min. In two cases the effect of AVJ modulation was relative; in one case the procedure was not effective but was repeated successfully 15 days later. In five cases the late effect was observed 18 – 24 hours following the procedure; in these instances we used a temporary pacemaker for the patient. In 48 cases we successfully achieved a "high level block" with a narrow QRS and a basic rhythm of 42 – 46 beats/min (bpm). Although such results are more favorable for the patient (there is no pacemaker dependence), the resumption of AV conduction could possibly be impeded; this was observed in five cases, four of which had high-level block. On average, we waited for 30 min for a possible resumption of AV conduction. A drug activation test was used; if the stable third-degree AV block or Frederic syndrome remained,

a DDDR or VVIR pacemaker (Metros, Kairos SR, Actros SR, and Kairos DR, all from Biotronik; Regency SR, Regency SR+, and Trilogy DR, all from Pacesetter, USA) was implanted (Figure 1). The initial postoperative procedures included:

- Pacemaker follow-up, threshold testing, and Holter-ECG monitoring;
- Echocardiographic investigation;
- Blood assays, i.e. creatin kinase-MB (CK-MB) fraction and troponin test);
- Patient interview.

These procedures were completed by the 7th post-operative day. The patient usually remained in the hospital for 8 – 9 days and was then discharged for subsequent outpatient treatment. The medications used during and following the postoperative period usually remained the same.

Results

Medications used in Group A were:

- Permanent AF: warfarin (3.0 – 4.5 – 6.0 mg); the international normalized ratio (INR) was kept between 2.0 – 3.0 – 3.5;
- Paroxysmal AF: aspirin; if contraindicated, ticlopidine, or clopidogrel was used; if paroxysms were frequent, warfarin was used;
- ACE inhibitors, usually perindopril or quinapril; if there were adverse effects, angiotensin II receptor blockers (e.g., candesartan) were used once a day;
- ß-blockers: metoprolol or bisoprolol were used once a day;
- Diuretics: K^+-sparring diuretics were used;
- Symptomatic treatment was individualized for each patient.

A similar drug scheme was used in Group B patients. Drug selection was determined by specialists familiar with outpatient dosage levels and conformed to the drugs covered by health insurance. Pacemaker follow-ups (Figures 2 and 3) and echocardiographic investigations were repeated at 3, 6, 12, 18, and 24 months following RFA procedure; the specific quality of life questionnaire was completed every 6 months. The currently available results demonstrate significant positive changes for the entire Group A.

Symptoms	Change (%)
Palpitations	-84
Exertion dyspnea	-38
Rest dyspnea	-57
Exercise tolerance	+42
Time to fatigue on exertion	+48
Chest discomfort	-64
NYHA class	-44

Table 7. Change in clinical parameters (mean value of all patients) several months after radiofrequency ablation.

The most rapid improvement occurred during the first year, after which the patients' condition stabilized. Patients were questioned regarding their subjective complaints, medication usage (both quantitative and qualitative in terms of improvement in health), ability to work, and amount of work. Medical expenses were also itemized for drug usage and cost (certain "pre-approved" drugs are determined by the Latvian Ministry of Welfare), travel expenses for doctor's visits, telephone calls to the doctor's office, and visits to in-patient and outpatient clinics. Almost all of the patients experienced a decrease in expenses.

Complaints regarding palpitations and other symptoms decreased dramatically (Table 7). About 58% of patients reported an increased ability to work, and 69% of patients had improved exercise tolerance. Drug use decreased by 50%.

Table 8 compares the number of postoperative hospitalizations and doctor visits for Group A before and after the RFA and pacemaker implantation procedures. Based on these criteria, we have shown that RFA combined with pacemaker implantation are effective methods for the treatment of highly symptomatic drug refractory AF. There was a notable difference for the ablated group before and after the procedures. Certainly this shows only one aspect of their problems. However, analysis of both patient groups has correctly shown the differences between RFA and pacemaker implantation in the long-term investigation of evidence-based methods for treating highly symptomatic drug refractory AF.

Up to now, the SF-36 questionnaire hasn't been analyzed in detail. Nevertheless, patients with permanent AF had lower scores on all subscales. Scores in general health, physical activity, vitality, and emotional

Type of visits	Before RFA	After RFA
Hospitalization per year (approximately)	3 – 8	0 – 1
Outpatient visits, emergency visits (approximately)	1 – 4	0 – 1
Urgent hospitalization	2 – 5	0 – 1
Visits to general practitioner, cardiologist	2 – 8	1 – 2

Table 8. Hospital visits before and after radiofrequency ablation.

well-being were markedly lower; no differences were observed in patients between 50 and 75 years of age.

One of our most successful procedures was performed on a 49-year-old former policeman, who had experienced myocarditis and AF from 1995 – 1997. In 1997 his condition deteriorated into permanent tachy-systolic AF. His left ventricular EF decreased to 37%; DC shocks and antiarrhythmic drug treatment were ineffective and congestive heart failure further complicated his health status. Conventional therapeutic strategies stabilized his condition, and he was categorized as NYHA class III-IV. During the winter of 1997 – 1998 the patient experienced two episodes of "cardiac asthma" with pulmonary edema; his psychological condition also deteriorated. The therapeutic methods of choice were RFA and pacemaker implantation. Today (Figure 2), 39 months after the procedures, his left ventricular EF is 56%; the left ventricular echocardiographic parameters have decreased, the patient has returned to work as an administrator, and he no longer experiences psychological problems.

Conclusion

Radiofrequency catheter ablation of the AVJ followed by implantation of a DDDR or a VVIR pacemaker is an effective treatment for stabilizing the heart rhythm of patients who suffer from chronic, drug refractory paroxysmal and permanent tachy-systolic atrial fibrillation, particularly following MVR. Although the methods are time-consuming and technically complicated, they are relatively simple from the medical point of view with only minimal complications. These methods improve patients' physical and mental health, quality of life, and ability to resume work. These methods must be considered as a positively balanced, economically motivated investment from both the State's and the patient's point of view.

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	SQ		NYHA		EF (%)		Drugs/day	
	before	after	before	after	before	after	before	after
Paroxysmal AF	3.2 ± 1.6	6.6 ± 0.6	3.1	1.9	47.1	51.4	6.4	3.2
Permanent AF	2.5 ± 1.1	7.7 ± 1.2	3.4	1.6	45.8	52.6	6.8	3.8

Table 9. Results from the quality of life questionnaire and clinical parameters before and after the radiofrequency ablation procedures in patients with paroxysmal and permanent atrial fibrillation (AF). SQ = specific quality of life questionnaire with 10 questions (the higher the score the better the patient's condition). EF = ejection fraction from Echo measurements.

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