

# Efficacy and Safety of Radiofrequency Catheter Ablation in Patients with Atrial Fibrillation

## *Eficacia y seguridad de la ablación por radiofrecuencia en pacientes con fibrilación auricular*

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### ABSTRACT

**Introduction:** Radiofrequency catheter ablation of atrial fibrillation is more effective than antiarrhythmic drugs for symptoms control, particularly in paroxysmal atrial fibrillation. The procedure is laborious and complex and not exempt from complications.

**Objective:** The aim of this study was to evaluate the outcomes of radiofrequency catheter ablation in a consecutive and selected population with recurrent atrial fibrillation refractory to antiarrhythmic drugs.

**Methods:** One-hundred and eleven patients (90 men) with paroxysmal (n = 75) or persistent (n = 36) atrial fibrillation, refractory to 2 (1.5-3) antiarrhythmic drugs were selected for radiofrequency catheter ablation. All the procedures were performed following a uniform methodology. Mean age was 56 ± 11 years, left atrial diameter was 41.5 (39-45) mm and left ventricular ejection fraction was 60% (56.5-66.5%). A total of 126 radiofrequency catheter ablation procedures were performed, including 15 second procedures, and 476/489 (97.3%) pulmonary veins were isolated. Twenty-five patients (22.5%) presented spontaneous ectopic activity in the pulmonary veins. Nonfatal complications occurred in 7/126 procedures (5.5%) and were satisfactorily resolved. Three patients presented vascular complications; other complications included one related to anesthesia, one subacute cardiac tamponade, one pericarditis without effusion and one pulmonary vein stenosis.

After 22-month follow-up (13-35 months), 83 patients (74.8%) remained in sinus rhythm without antiarrhythmic drugs. The remaining 28 patients (25.2%) presented recurrences. Four of these patients had a favorable response to these previously inefficient drugs, 8 had atrial fibrillation in spite of receiving antiarrhythmic drugs and 1 patient will undergo a new ablation. The remaining 15 patients underwent a second ablation procedure; 10 of them are recurrence-free after 12 (9-31) months.

**Conclusion:** In this consecutive series of patients with atrial fibrillation refractory to drugs, radiofrequency catheter ablation showed an adequate rate of success and low level of complications.

**Key words:** Catheter Ablation - Atrial Fibrillation - Follow-Up Studies.

### RESUMEN

**Introducción:** La ablación por radiofrecuencia de la fibrilación auricular es más eficaz que las drogas antiarrítmicas en el control de los síntomas, particularmente cuando la arritmia es paroxística. Consiste en un procedimiento laborioso y complejo no exento de complicaciones.

**Objetivo:** Evaluar los resultados de la ablación por radiofrecuencia en una población seleccionada consecutiva con fibrilación auricular recurrente y refractaria a drogas antiarrítmicas.

**Material y métodos:** Se evaluaron 111 pacientes, 90 hombres, con fibrilación auricular paroxística (n = 75) o persistente (n = 36), refractaria a 2 (1,5-3) drogas antiarrítmicas que fueron seleccionados para la ablación por radiofrecuencia. Todos los procedimientos se realizaron siguiendo una metodología uniforme. La edad fue de 56 ± 11 años, con un diámetro de la aurícula izquierda de 41,5 (39-45) mm y fracción de eyección del ventrículo izquierdo del 60% (56,5-66,5%). Se realizaron 126 procedimientos de ablación por radiofrecuencia, incluyendo 15 segundos procedimientos. Se aislaron 476/489 (97,3%) venas pulmonares. Veinticinco pacientes (22,5%) presentaron actividad ectópica espontánea de las venas pulmonares. Se presentaron complicaciones no mortales en 7/126 procedimientos (5,5%), que se resolvieron satisfactoriamente. Tres pacientes presentaron complicaciones vasculares y se observó una complicación anestésica, un taponamiento cardíaco subagudo, una pericarditis sin derrame y una estenosis de vena pulmonar. Luego de un seguimiento de 22 (13-35) meses, 83 pacientes (74,8%) se mantuvieron en ritmo sinusal sin drogas antiarrítmicas. Los 28 pacientes restantes (25,2%) presentaron recurrencias. Cuatro de ellos respondieron satisfactoriamente a estas drogas (previamente ineficaces), ocho tuvieron fibrilación auricular a pesar de recibir drogas antiarrítmicas y 1 paciente se encuentra en plan de reablación. A los 15 pacientes restantes se les realizó un segundo procedimiento de ablación. Diez de ellos se mantienen sin recurrencias luego de 12 (9-31) meses.

**Conclusión:** En esta serie consecutiva de pacientes con fibrilación auricular refractaria a drogas antiarrítmicas, la ablación por radiofrecuencia mostró una tasa de éxito adecuada y un nivel bajo de complicaciones.

**Palabras clave:** Ablación por catéter - Fibrilación auricular - Estudios de seguimiento.

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## Abbreviations

<b>3D</b>	Three-dimensional	<b>AF</b>	Atrial fibrillation
<b>AFL</b>	Atrial flutter	<b>LMWH</b>	Low-molecular-weight heparin
<b>LA</b>	Left atrium	<b>NOACs</b>	New oral anticoagulants
<b>RCA</b>	Radiofrequency catheter ablation	<b>LAA</b>	Left atrial appendage
<b>RCA-AF</b>	Radiofrequency catheter ablation of atrial fibrillation	<b>TSP</b>	Transseptal puncture
<b>CAFEs</b>	Complex atrial fractionated electrograms	<b>CS</b>	Coronary sinus
<b>AADs</b>	Antiarrhythmic drugs	<b>PV</b>	Pulmonary vein
<b>TEE</b>	Transesophageal echocardiography		

## INTRODUCTION

Atrial fibrillation (AF) is one of the most prevalent arrhythmias in clinical practice, provoking high morbidity and mortality, more hospitalizations and increased health care expenditure. (1-3) From the moment the pathophysiology of this arrhythmia, which may be produced by triggers or ectopic beats originating in the pulmonary veins (PVs), was understood, radiofrequency catheter ablation (RCA) has shown better results than antiarrhythmic drugs (AADs) in terms of recurrences or improved symptoms, particularly in paroxysmal AF. (4-6)

Radiofrequency catheter ablation of atrial fibrillation (RCA-AF) has become one of the most challenging interventional cardiology procedures, requiring availability of technology and formation in invasive electrophysiology. The success of the procedure and the incidence of complications, even severe and fatal, are variable and depend on many factors. In the last Argentine Catheter Ablation Registry, RCA-AF occupied the sixth place of treated arrhythmias, probably due to the technology required and professional experience rather than to the prevalence of the arrhythmia. (7) For these reasons, it is important to become aware of and communicate the outcomes of this technique in our environment.

The aim of the present study was to report the outcomes and complications in a series of consecutive symptomatic patients with recurrent AF, refractory to AADs, who were treated with RCA.

## METHODS

### Inclusion criteria

The study was performed between January 2010 and August 2013 and included consecutive patients with recurrent paroxysmal or persistent nonvalvular AF, refractory to at least one class IC or III AAD. Patients > 75 years and those with left atrial (LA) anteroposterior diameter > 55 mm were excluded, and patients with heart failure were referred for the procedure only when tachycardia-induced cardiomyopathy was suspected.

### Pre-procedural protocol

All patients underwent multislice computed tomography scanning within 3 months before ablation for anatomical reconstruction in the three-dimensional (3D) navigation system. Oral anticoagulant agents were administered for one month before the procedure. New oral anticoagulants (NOACs) were discontinued 24 hours before the procedure.

Patients treated with vitamin K antagonists were switched to bridging low-molecular weight heparin (LMWH) 48-72 hours before catheter ablation. Antiarrhythmic drugs were discontinued for 5 half-lives with the exception of amiodarone in persistent AF. All the patients underwent transesophageal echocardiography (TEE) before and/or during the procedure to rule out LA thrombi and to eventually guide the transseptal puncture (TSP).

### Catheter ablation procedure

The procedure was performed using 3D ENSITE-NAVX, version 8 navigation system (St. Jude Medical) and recorded on a 36-channel polygraph (Exxer). In all cases, the procedure was performed under general anesthesia, with noninvasive blood pressure and central venous pressure control and esophageal temperature monitoring.

Multipolar catheters were introduced via the right femoral vein, right jugular vein and/or left femoral vein and positioned in the coronary sinus (CS) and bundle of His. The TSP was performed under fluoroscopic guidance with or without TEE using the one-puncture, double-transseptal catheterization technique. A 20-pole circular catheter and an externally irrigated-tip ablation catheter were placed in the LA. Fractionated heparin (100 U/kg) was then administered to maintain the activated clotting time between 350 and 400 seconds. Radiofrequency energy was applied at 30-35 W with maximum temperature of 43 °C, and was reduced to 25 W in the posterior wall when esophageal temperature increased  $\geq 0.5$  °C.

The LA, PVs and left atrial appendage (LAA) anatomy was reconstructed and was used to guide catheter navigation (Figure 1).

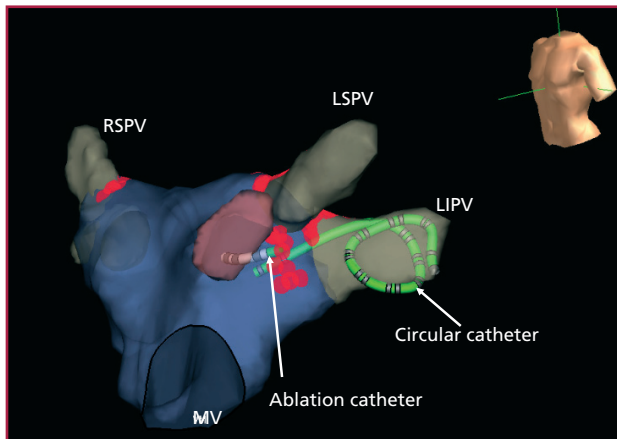
The bidirectional conduction between the PVs and the LA was evaluated using the circular catheter during sinus rhythm and during CS, PV and/or LAA pacing. These tests were performed before and after treatment.

Radiofrequency was delivered encircling each PV until bidirectional isolation was obtained. Additional energy was applied to the sites of block. In some patients with difficult isolation or premature beats triggering AF, adenosine or isoproterenol was used to evaluate reconnection and other triggers. Thirty minutes after energy was delivered, the isolation of each PV was evaluated.

In cases of persistent AF, additional ablation of complex atrial fractionated electrograms (CAFEs) was performed using a map generated by the 3D navigator. The patients who remained in AF after the procedure underwent electrical cardioversion.

### Post-procedural protocol

All patients were admitted to the coronary care unit for 24 hours. New oral anticoagulants were restarted 12/24 hours after the procedure, in the absence of pericardial effusion.



**Fig. 1.** Anatomical image of the left atrium and the pulmonary veins generated by the three-dimensional navigator in cephalic left anterior oblique view. A circular catheter in the left inferior pulmonary vein and an ablation catheter can be seen during radiofrequency delivery. The red round dots represent the area where radiofrequency was applied. MV: Mitral valve. LIPV: Left inferior pulmonary vein. RSPV: Right superior pulmonary vein. LSPV: Left superior pulmonary vein.

For patients receiving vitamin K antagonists, half-dose LMWH was administered 4-6 hours after the procedure in the absence of complications. The following day, after echocardiographic evaluation, full-dose heparin was administered and oral anticoagulant therapy was started.

Anticoagulation and antiarrhythmic therapy was continued for 3 months. The patients underwent clinical assessment, ECG evaluation and 24-hour Holter monitoring once a month during the first 3 months, every 3 months during the first year and then every 6 months. The first 3 months were considered a blanking period and any episode of AF was not considered as recurrence. After this period, any episode of AF or atrial flutter (AFL) lasting > 30 seconds was considered as recurrence.

Major complications were defined as those extending hospital stay or requiring any intervention.

### Statistical analysis

Discrete variables are expressed as percentages. Continuous variables with normal distribution are expressed as mean  $\pm$  standard deviation or median and 25-75% interquartile range for non-Gaussian distribution. The results were compared using the chi-square test for discrete variables or Student's t test or Wilcoxon rank sum test for continuous variables, as applicable. A p value < 0.05 was considered statistically significant.

### RESULTS

A total of 111 patients were included in the study. Mean age was  $56 \pm 11$  years, 90 patients were men and 51% had hypertension. Seventy-five patients presented paroxysmal AF, 34 persistent AF, and 2 long-standing persistent AF with tachycardia-induced cardiomyopathy, refractory to 2 (1.5-3) AADs (Table 1). Twenty-eight patients (25.2%) received NOACs. Left atrial diameter was 41.5 mm (39-45) and left ventricular ejection fraction was 60% (56.5-66.5%).

### Results of the catheter ablation procedure

A total of 126 radiofrequency catheter ablation procedures were performed, including 15 second procedures. Out of 489 PVs, 476 (97.3%) were isolated and in 116 procedures all the PVs were isolated (92%). Spontaneous premature beats in at least one PV were observed in 25/111 patients (22.5%). The procedure lasted 245 (219-300) minutes and fluoroscopy time was 60 (51-70) minutes.

In patients with persistent AF (n = 36), in addition to electrical PV isolation, radiofrequency was applied in areas with CAFE. All these patients required electrical cardioversion to revert to sinus rhythm.

In 7/126 procedures (5.5%) non-fatal major complications occurred, with complete resolution. One patient presented stenosis of a PV that required stent implantation. One patient presented subacute cardiac tamponade 6 hours after the procedure that resolved with percutaneous drainage. These two complications occurred in the first 10 procedures performed. Three patients presented vascular complications (2 pseudoaneurysms of the femoral veins and 1 arteriovenous fistula), two of which required surgical repair. One patient suffered a post-procedural anesthesia-related complication requiring mechanical ventilation, and another patient presented pericarditis without effusion that resolved with medical treatment.

### Follow-up

At 22-month follow-up (13-35 months), 83 patients (74.8%) remained in sinus rhythm without AADs. The remaining 28 patients (25.2%) presented recurrences at 6.5 - (4-13) month follow-up (Figure 2). Four of these patients are free of arrhythmia under AADs (which were previously ineffective), the percentage of patients free of AF/AFL increasing to 78.4% after a single ablation procedure. Eight patients have AF despite antiarrhythmic treatment (4 paroxysmal AF and 4 permanent AF) and one patient is scheduled for repeat catheter ablation.

**Table 1.** Population characteristics

Baseline characteristics	n = 111
Age, years	56 $\pm$ 11
Male gender, n (%)	90 (81)
Hypertension, n (%)	57 (51)
Paroxysmal AF, n (%)	75 (67.6)
Persistent AF, n (%)	34 (30.6)
Long-lasting persistent AF, n (%)	2 (1.8)
Antiarrhythmic drugs	2 (1.5-3)
Left atrial diameter, mm	41.5 (39-45)
Ejection fraction, %	60 (56.5-66.5)

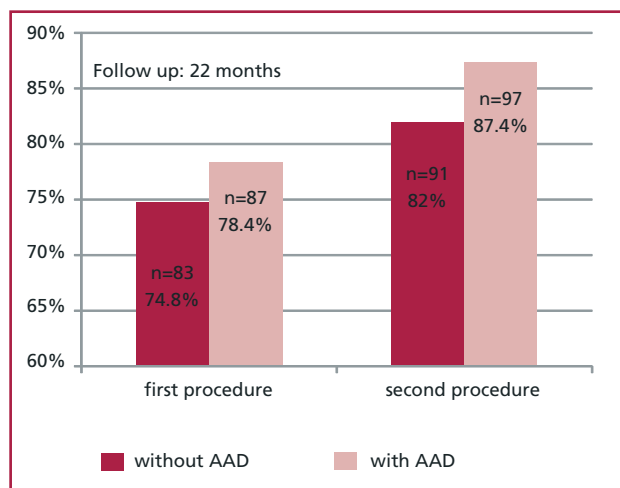
Discrete variables are shown as n (%). Continuous variables are expressed as median and interquartile range, except for age (mean  $\pm$  standard deviation). AF: Atrial fibrillation.

The remaining 15 patients underwent a second ablation procedure, with two patients in sinus rhythm within the 3 month-blanking period. Of the 13 remaining patients, 10 are free of AF/AFL (8 without AADs and 2 with AADs) 12 (9-31) months after the second procedure (Figure 2). Three patients presented recurrences (2 treated with AADs and 1 scheduled for a third procedure). Therefore, the rate of sinus rhythm maintenance after two procedures was 82% without AADs and 87.4% with AADs.

Table 2 shows the different clinical characteristics according to the type of AF. Patients with persistent AF had a greater prevalence of hypertension and larger LA diameter. The recurrence rate was lower in patients with paroxysmal AF (17/75, 22.7%) compared with those with persistent AF, but this difference was not significant [(11/36, 30.6%), OR 0.66 (0.27-1.62); p = 0.37]. No other clinical (e. g., gender, age, hypertension, left ventricular ejection fraction or LA size) or procedure-related parameters (e. g., PV ectopic beats, impossibility to isolate all the PVs or procedure duration) were associated with increased recurrence rate.

**DISCUSSION**

In the present study, RCA-AF in a population of con-



**Fig. 2.** Diagram representing the outcome free of atrial fibrillation in the first and second procedure, without antiarrhythmic drugs and with antiarrhythmic drugs.

secutive patients, using a homogeneous technique, shows similar results to those published in the international literature.

The 74.8% rate of sinus rhythm maintenance during follow-up after an ablation procedure is similar to the one reported by international studies, ranging between 60% and 85%. (8, 9) In our country, the only publication with this procedure on 94 patients showed a final success rate of 84%, (10) similar to the one obtained in our study (82%) with a longer follow-up period. In accordance with other reports, the success rate with a second procedure increased the possibility of sinus rhythm maintenance. (9)

The good results of our study depend on multiple factors. From a technical perspective, the same 3D navigation system used in all the cases allowed better management, a group of experienced operators conducted the procedures, and an externally irrigated-tip ablation catheter producing deeper lesions with less local thrombosis was used. (8) It is also important to mention that the rate of PV electrical isolation was high (>95%), insisting on achieving bidirectional block of the veno-atrial junction, even with adenosine test in some cases which can unmask latent conduction in the site of block. (11-13) Perfect isolation is a key condition to warrant a good result, as conduction reconnection of at least one PV is a constant in patients with recurrences. (14)

The other factor that should be mentioned was that most of the patients selected had paroxysmal AF without heart disease. The information about the pathophysiology of AF is still incomplete. However, it is accepted that the ectopic activity of the PVs plays a key role in the paroxysmal forms, especially in the normal heart or with mild heart disease. (4, 5, 9) In our population, this is reflected by the low average age (56 years) and the low incidence of heart disease with a mildly enlarged LA. It is worth noting that in younger patients (< 40 years) AF may be really secondary to PV tachycardia with fibrillatory conduction towards the LA (Figure 3). In these cases, isolation of the responsible PV as single therapy has demonstrated good results. (15)

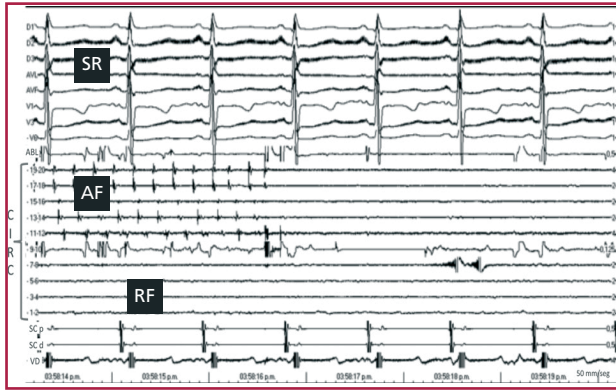
The mechanism of persistent AF is more complex; in addition to PV triggers, other factors may interact, such as atrial rotors, and LAA, superior vena cava or

	Paroxysmal AF (n = 75)	Persistent AF (n = 36)	p
Age, years	57 (45-66)	60 (53-64)	0.23
Male gender, %	81.3	80.6	0.922
Follow-up, months	22 (13-33)	20 (11-34)	0.426
Hypertension, %	43.7	65.7	0.032
LA diameter, mm	41 (38-43)	44 (40-47)	0.048
LVEF, (%)	60 (60-67)	58 (49-69)	0.373
Recurrence, %	22.7	30.6	0.37
Time to recurrence, months	5.5	8.5	0.345

LA: Left atrium AF: Atrial fibrillation. LVEF: Left ventricular ejection fraction. Continuous variables are expressed as median and interquartile range.

**Table 2.** Characteristics and outcomes by type of atrial fibrillation

CS triggers, probably as a consequence of atrial electrical remodeling. (8) In these cases, our technique consisted in adding ablation of fractionated electrograms. These signals might represent sites of slow conduction and/or rotors with influence in maintaining AF. (16-18)



**Fig. 3.** Intracardiac electrogram during radiofrequency (RF) delivery with surface electrocardiogram (LI to V6). The patient remains in sinus rhythm (SR) in the electrocardiogram, but the pulmonary vein electrogram shows atrial fibrillation (AF) that is not conducted to the rest of the LA due to the ablation effect, and reverts during radiofrequency application

Recurrences were observed in 28 patients. This phenomenon is mainly due to reconnection between the PV and the LA, as demonstrated in our study. After catheter ablation, the good response to AADs that were previously ineffective is a common finding, very probably associated to substrate changes caused by the application of radiofrequency.

We did not identify key factors for the development of recurrences; yet, we observed a nonsignificant trend in persistent AF. In this group, 94% of patients had AF for less than one year, and only 2/36 had persistent long-lasting AF, which is associated with higher recurrence rate. We did not notice any important clinical differences between patients with paroxysmal AF and persistent AF, which may in part explain their similar outcome. A greater number of patients could have shown significant differences in the recurrence rate. We cannot rule out that closer monitoring (with an implantable loop or telemonitoring) could have revealed higher recurrence.

In these patients, predictors of recurrences should be investigated. The detection of atrial fibrosis by delayed gadolinium-enhanced magnetic resonance imaging could be a key variable impacting in ablation outcome. (19) In those with >20% wall fibrosis, recurrences may be above 80% and the role of ablation would be minimal.

The low incidence of complications in our study is mainly due to the same reasons which influenced success: the selection of young patients with mild heart disease and the presence of paroxysmal forms requiring a less amount of radiofrequency. However,

according to large international series, the percentage of complications is not significantly higher in patients with persistent AF. The rate of complications is two times greater in patients > 70 years. (20, 21)

The complications of vascular access sites are more frequent than in ablation of supraventricular tachycardia, probably associated to the higher level of anticoagulation required. (22)

The lack of embolic accidents may be related to technical issues as maintenance of an activated clotting time > 350 seconds, using a single sheath and displacing it to the right atrium during part of the procedure. Studies with intracardiac echocardiography have demonstrated local thrombi on sheath tips. (23) Other important aspects include the use of externally irrigated-tip ablation catheters which reduce local thrombosis, and the strict control of bubbles on the guide wires. (8) The studies show that most embolisms resolve completely and mostly develop with persistent AF. (24)

Stenosis of the pulmonary vein is uncommon; in our case, it required a stent implant in only one patient who remained with sinus rhythm and free of symptoms after 2 years.

The most serious complications occurred at the beginning of the learning curve. Recently, a registry of 90,000 ablations in the United States confirmed that the operator's experience is the most important variable associated with complications, particularly when it is lower than 25 procedures/year. (25) Our group has exceeded this number in the last two years. There were no deaths in this series. Fatal events in RCA-AF are mostly associated with cardiac tamponade and, to a less extent, to atrioesophageal fistula. (21) Our rate of cardiac tamponade (0.8%) is similar to the one reported worldwide. (21) Transseptal puncture must be performed with particular care and guided by TEE in difficult cases, to prevent left atrial appendage perforation where 3D navigation is mostly helpful. The usefulness of esophageal temperature monitoring is not completely demonstrated, in part due to the uncommon incidence of fistula (0.06%). Yet, this technical aspect was important, as radiofrequency delivery was interrupted when the temperature increased, power was reduced and the catheter was displaced every 5-10 minutes, all maneuvers which have demonstrated to reduce the development of lesions in the esophageal mucosa. (26, 27)

Finally, we consider that treatment of AF is multifactorial, and ablation has a clearer role in the early stages. (28) Patients should be advised of the risks and benefits of RCA-AF, and consider the possibility of undergoing a second procedure which increases sinus rhythm maintenance.

## CONCLUSIONS

In this consecutive series of patients with AF, radiofrequency catheter ablation proved to be an effective method with rate of success within international

standards and low incidence of complications.

#### Conflicts of interest

None declared.

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