Atrial Fibrillation Ablation by Use of Electroanatomical Mapping: Efficacy and Recurrence Factors

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Resumo

Background: Radiofrequency catheter ablation guided by electroanatomical mapping is currently an important therapeutic option for the treatment of atrial fibrillation. The complexity of the procedure, the several techniques used and the diversity of the patients hinder the reproduction of the results and the indication for the procedure.

Objective: To evaluate the efficacy and factors associated with recurrence of atrial fibrillation.

Methods: Prospective cohort study with consecutive patients submitted to atrial fibrillation ablation treatment guided by electroanatomical mapping. The inclusion criteria were as follows: minimum age of 18 years; presence of paroxysmal, persistent or long-standing persistent AF; AF recording on an electrocardiogram, exercise testing or Holter monitoring (duration longer than 15 minutes); presence of symptoms associated with AF episodes; AF refractoriness to, at least, two antiarrhythmic drugs, one of which being amiodarone, or impossibility to use antiarrhythmic drugs.

Results: The study included 95 patients (age 55 ± 12 years, 84% men, mean CHADS2 = 0.8) who underwent 102 procedures with a median follow-up of 13.4 months. The recurrence-free rate after the procedure was 75.5% after 12 months. Atrial fibrillation recurred as follows: 26.9% of patients with paroxysmal and persistent atrial fibrillation; 45.8% of patients with long-standing persistent atrial fibrillation (p = 0.04). Of the analyzed variables, the increased size of the left atrium has proven to be an independent predictor of atrial fibrillation recurrence after the procedure (HR = 2.58; 95% CI: 1.26-4.89). Complications occurred in 4.9% of the procedures.

Conclusion: Atrial fibrillation ablation guided by electroanatomical mapping has shown good efficacy. The increase in left atrium size was associated with atrial fibrillation recurrence. (Arq Bras Cardiol. 2014; 102(1):30-38)

Keywords: Arrhythmias, Cardiac; Atrial Fibrillation; Catheter Ablation; Heart Atria.

Introduction

Atrial fibrillation (AF) is the most common persistent arrhythmia in clinical practice, affecting approximately 1.5% to 2% of the population in developed countries, with a still increasing mean age, currently ranging from 75 to 85 years[1]. In Brazil, around 1.5 million individuals are estimated to have AF, which is considered to account for 33% of all hospitalizations due to arrhythmia, being associated with an increased risk for encephalic vascular accident (EVA), heart failure (HF) and overall mortality[2].

Ablation of AF is increasingly becoming an important therapeutic option[3]. The complexity of the procedure, the diversity of techniques used in ablation and of patients with AF and their different pathogenicities hinder the reproduction of results and the indication for the procedure[4]. Recurrence of AF remains the major hindrance to the results of AF ablation, and the mechanisms involved and markers have not been totally clarified.

Since the contribution by Haïssaguerre[5], emphasizing the value of ectopic foci in pulmonary veins (PV) as an important factor in AF physiopathogenesis, a new perspective for the treatment of that arrhythmia by using a catheter has emerged. The clinical experience acquired over recent years along with technological advances have provided greater safety and efficacy to the treatment of AF. In that context, tridimensional mapping has become an important tool to the electrophysiologist regarding catheter anatomy and location, providing a safe and effective treatment of the lesions inside the left atrium (LA) and around the PV[6].

This study aimed at assessing the efficacy of AF ablation by use of a radiofrequency (RF) catheter guided by electroanatomical mapping, and the factors related to AF recurrence.

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Methods

Study design

This is a prospective cohort study including consecutive patients submitted to RF catheter ablation guided by electroanatomical mapping for the treatment of AF.

Population

The present study was performed at the Arrhythmia Service of the Hospital São Lucas (HSL) of the Pontifícia Universidade Católica of Rio Grande do Sul (PUC-RS), in the city of Porto Alegre, state of Rio Grande do Sul, from April 2007 to March 2012. This study included 95 patients, who underwent RF catheter ablation guided by electroanatomical mapping for the treatment of AF (total of 102 procedures). The patients' inclusion criteria were as follows: minimum age of 18 years; presence of paroxysmal, persistent or long-standing persistent AF; AF recording on an electrocardiogram (ECG), exercise testing or Holter monitoring (duration longer than 15 minutes); presence of symptoms associated with AF episodes; AF refractoriness to, at least, two antiarrhythmic drugs, one of which being amiodarone, or impossibility to use antiarrhythmic drugs. The exclusion criteria were as follows: presence of a thrombus in the LA; contraindication to anticoagulation; and not providing written informed consent.

This study project was approved by the Committee on Ethics and Research of the Instituto de Cardiologia do Rio Grande do Sul/Fundação Universitária de Cardiologia (protocol 103.749).

Data collection and follow-up

After the patients provided written informed consent, all information regarding their clinical data and procedures were prospectively collected. The patients were clinically followed up, and underwent ECG and 24-hour Holter monitoring on day 30, and at 3, 6, 18 and 24 months. The results were assessed independently of the clinical follow-up normally performed and by observers not related to the procedure, to reduce possible biases inherent in data collection.

Ablation procedure

All patients underwent transesophageal echocardiography before the procedure. From 2010 on, the patients also underwent computed tomographic angiography prior to the procedure, enabling the integration of the tomographic images with the mapping system (Cartomerge, Biosense Webster Inc). Patients on warfarin had their medication adjusted to undergo the procedure, with an International Normalized Ratio (INR) between 1.5 and 2.5. The LA was approached through two transseptal punctures guided by intracardiac echocardiogram to place a Lasso catheter (Cordis Corporation, Biosense Webster) and a catheter irrigated with saline solution with a 3.5-mm tip (NaviStar, ThermoCool, Biosense Webster), used for geometrical reconstruction and ablation. Later, an intravenous bolus of 10,000 U of unfractionated heparin was administered, being followed by activated coagulation time assessments every 30 minutes, aiming at maintaining that time between 250 and 350 seconds.

Point-to-point ablation lines were placed around the PV and 1 to 2 cm from their ostia. The RF was applied with a potency of 25-30 W and at a maximum temperature of 45º C, being kept until achieving a 50% decrease in the amplitude of the atrial electrogram located in the ablation area or until reaching an electrogram < 0.1 mV. The procedure was considered successful when complete isolation of the PV was achieved, including PV entrance and exit block. Entrance block was defined as the absence or dissociation of the potentials of the PV, through atrial stimulation or sinus rhythm. Exit block was identified as the inability of the PV electrical activity to achieve the LA during electrical stimulation inside the PV. After demonstrating the PV electrical isolation, there was a 20-minute wait to observe whether there was reconnection of any PV. In cases of persistent AF or long-standing persistent AF, and those with persistent AF after the electrical disconnection of the PV, additional ablation lines were sequentially performed in the mitral isthmus, in addition to gathering the lines in the LA roof, at the LA base and inside the coronary sinus, until AF reversion. When no spontaneous reversion was achieved, electrical cardioversion was attempted. When reversion was achieved, the procedure was interrupted. In case of no reversion, additional RF applications were performed at fractionated potentials on the posterior wall. Again, an electrical cardioversion was performed, followed by procedure interruption. The procedure was considered to fail when the initial success above described was not achieved or when no AF reversion was obtained, even with electrical cardioversion. The venous sheaths were withdrawn after the end of the procedure, reaching an activated coagulation time shorter than 180 seconds, either spontaneously or by using protamine. Intravenous continuous heparin was initiated 6 hours after removing the sheaths and maintained for 24 hours, being then replaced by low-molecular-weight heparin until reaching an INR greater than 2 with warfarin.

Definition of the variables

Atrial fibrillation was classified according to the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology[7], and the variables were related to the procedure according to the HRS/EHRA/ESC[8]. Atrial fibrillation is considered paroxysmal when self-terminating, usually within 48 hours, but may continue for up to 7 days. Atrial fibrillation is considered persistent when an episode lasts more than 7 days or requires termination by cardioversion. Atrial fibrillation is considered long-standing persistent if it has lasted for ≥ 1 year when it is decided to adopt a rhythm control strategy. The patient was considered recurrence-free when neither AF, atrial flutter nor atrial tachycardia occurred within 30 days from the procedure and during the follow-up. Recurrence in the first 30 days were recorded; however, they were not included as recurrence for the major outcome.

Major complications were considered when resulting in permanent sequela, death, need for therapeutic intervention or prolongation of hospitalization. The clinical importance of AF was estimated according to the EHRA score[9].

Statistical analysis

Continuous variables were expressed as mean and standard deviation, and Student *t* test was used to compare the differences. Chi-square test and Fisher exact test were used to assess the differences between categorical variables. The recurrence rate was assessed by using the Kaplan-Meier curve,

and the significance analysis between variables (univariate) was performed with the long-rank test. The variables showing association with the outcome at a p value < 0.10 or those with clinical importance related to the outcome AF recurrence after ablation were selected for Cox regression. The two-tailed p value < 0.05 was considered statistically significant, and the results of Cox regression were expressed as the incidence density ratio (HR) and its respective 95% confidence intervals (CI). The analysis was performed with the Statistical Package for the Social Science (SPSS) program, version 20.0.

Results

Characteristics of the population

This study assessed 102 procedures for AF ablation in 95 patients, mainly men, with paroxysmal AF of low risk for thromboembolic events. Table 1 shows the major characteristics of the population studied.

No patient had heart valve disease, asymmetric hypertrophic cardiomyopathy, or severe kidney failure (creatinine clearance < 40 mL/min). Most patients (85) were on antiarrhythmic drugs as follows: amiodarone, 48 (56.5%); propafenone, 15 (17.6%); sotalol, 5 (5.9%); and two or more antiarrhythmic drugs, 17 (20.0%). Forty-nine patients (51.6%) had already undergone at least one electrical cardioversion and 66 (69.5%) had already been hospitalized due to AF in the previous 12 months.

Table 1 - Characteristics of the population studied

Characteristics	n = 95
Age (years)	55.5 ± 12.1
Sex (male)	80 (84.2)
AF classification	
Paroxysmal	62 (65.3)
Persistent	12 (12.6)
Long-standing persistent	21 (22.1)
EHRA (mean)	2.4 ± 0.8
1	13 (13.7)
2	36 (37.9)
3	40 (42.1)
4	6 (6.3)
SAH	46 (48.4)
DM	8 (8.42)
HF	5 (5.26)
$CHADS_2$ (mean)	0.8 ± 0.9
0	42 (44.2)
1	35 (36.8)
2	11 (11.6)
3	6 (7.4)
LA diameter (mm)	43 ± 5
Ejection fraction (%)	66 ± 9

Data expressed as mean ± standard deviation or n (%). AF: atrial fibrillation; EHRA: European Heart Rhythm Association; SAH: systemic arterial hypertension; DM: diabetes mellitus; HF: heart failure; LA: left atrium.

Procedure

Table 2 shows the major characteristics of the procedures performed in this study. Six patients required a second procedure, and only one patient required a third one. Most patients had sinus rhythm by the end of the procedure.

Complete isolation of the PV was achieved in 89.7% of the procedures.

Figure 1, comparing the total durations of the procedures and radioscopy between the initial years and more recent ones, shows a progressive decrease of both total durations ($p < 0.001$ and $p < 0.001$, respectively), according to the linear trend test. Between the years 2009 and 2012, the period corresponding to the greatest number of procedures, there was an 18-minute/year reduction in the total duration of the procedure ($p = 0.001$) and a 6.6-minute/year reduction in the total duration of radioscopy ($p = 0.005$).

Efficacy of the procedure

The median follow-up duration was 13.4 months. The recurrence-free rate for patients undergoing AF ablation guided by electroanatomical mapping was 75.5% in 12 months (Figure 2). There were 33 recurrences, whose median time was 8 months. The percentage of patients not using antiarrhythmic drugs among those free from recurrence was 33.3% at 3 months, 66.7% at 6 months, and 88.2% at 18 months of follow-up.

Variables associated with AF recurrence

Table 3 shows the patients' major clinical characteristics related to the procedure, stratified by the outcome recurrence.

The variable 'AF classification' was divided into paroxysmal AF + persistent AF (total of 78 procedures, and

Table 2 - Characteristics of the ablation procedures

Characteristics	n = 102
Duration of procedure (min)	167 ± 50
Duration of radioscopy (min)	51 ± 18
Number of procedures	
1	95 (93.1)
2	6 (5.9)
3	1 (1.0)
Final rhythm	
Spontaneous sinus	77 (75.5)
Sinus after ECV	15 (14.7)
AF	10 (9.8)

Data expressed as mean ± standard deviation or n (%). ECV: electrical cardioversion; AF: atrial fibrillation.

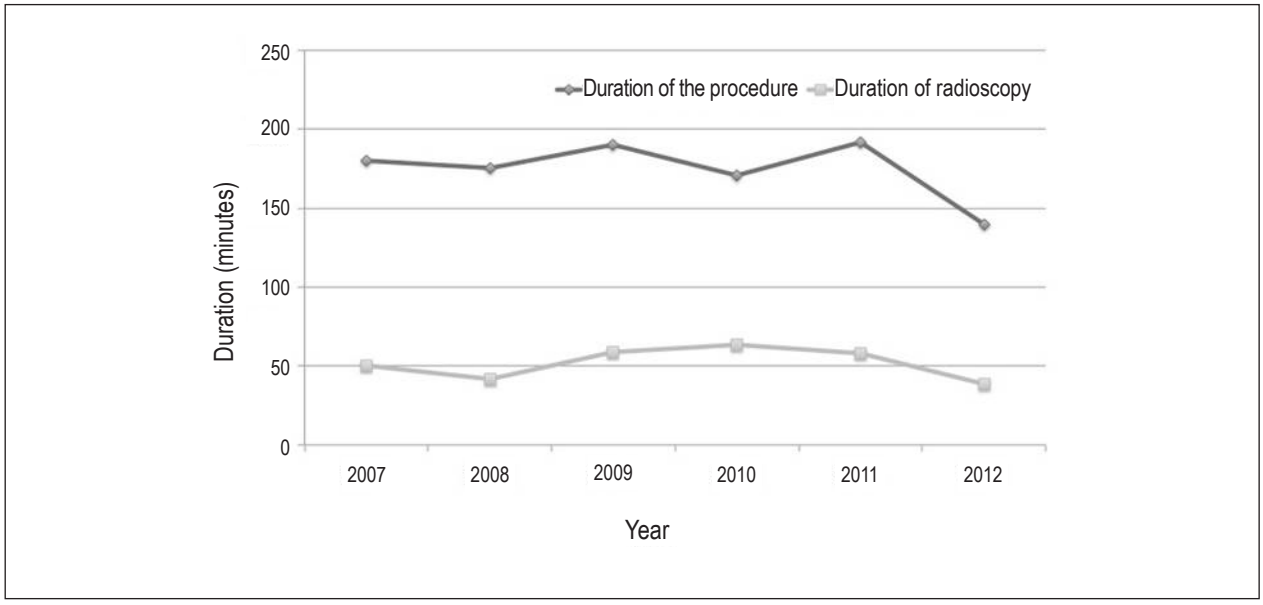


Figure 1 - *Mean duration of the procedure and of radioscopy according to the year the procedure was performed.*

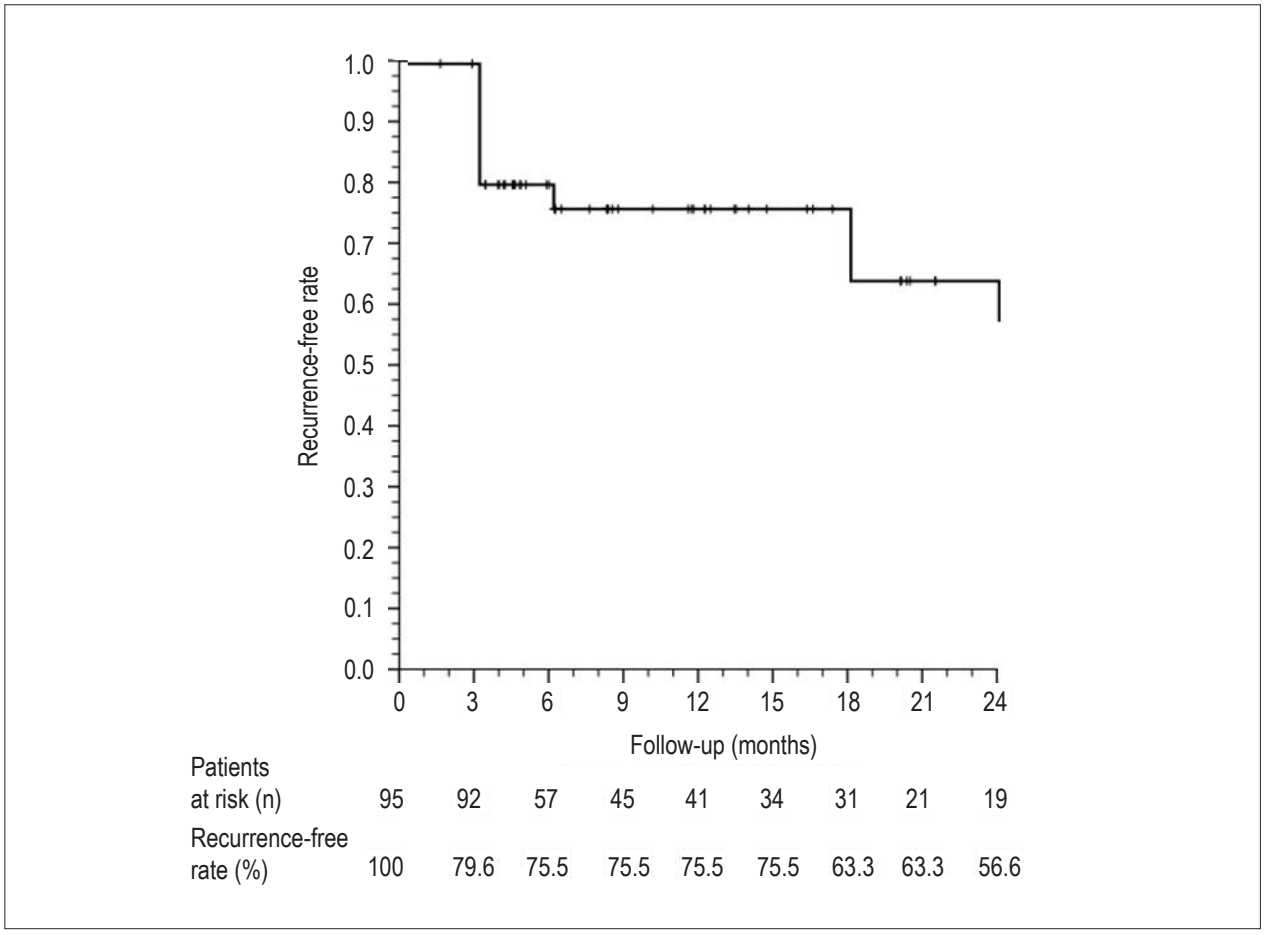


Figure 2 - *Kaplan-Meier curve for atrial fibrillation recurrence.*

Table 3 - Clinical characteristics related to the procedure, stratified according to atrial fibrillation recurrence

Characteristics	No AF recurrence (n = 69)	AF recurrence (n = 33)	P value
Age (years)	55.5 ± 12	55.7 ± 10	0.91
Sex (male)	58 (84.1)	29 (87.9)	0.76
AF classification			
Paroxysmal	47 (68.1)	19 (57.6)	
Persistent	10 (14.5)	2 (6.1)	0.96
Long-standing persistent	13 (18.8)	11 (33.3)	
SAH	34 (49.3)	17 (51.5)	0.83
CHADS2 (mean)	0.75 ± 0.8	0.87 ± 0.9	
0	31 (44.9)	13 (39.4)	
1	26 (37.7)	13 (39.4)	0.50
2	8 (11.6)	3 (9.1)	
3	3 (4.3)	3 (9.1)	
LA diameter (mm)	41 ± 4	48 ± 4	0.001
Ejection fraction (%)	66 ± 9	66 ± 6	0.91
Duration of procedure	151 ± 50	187 ± 56	0.001
Duration of radioscopy	47 ± 19	58 ± 15	0.44

Data expressed as mean ± standard deviation or n (%).
AF: atrial fibrillation; SAH: systemic arterial hypertension; LA: left atrium.

recurrence rate per procedure of 26.9% in the follow-up time) and long-standing persistent AF (total of 24 procedures, and recurrence rate per procedure of 45.8%) (p = 0.04).

After adjusting for age, sex, AF classification, presence of systemic arterial hypertension (SAH), CHADS2 score, and ejection fraction, the size of the LA showed to be an independent predictor of AF recurrence after the procedure, with a HR of 2.58 (95% CI: 1.36-4.89) per adjusted millimeter.

The variable 'size of the LA' was divided into three groups based on the median (42 mm) and 75th percentile (46 mm) of the sample as follows: Group 1 (G1), composed by LA size between 34 and 42 mm; Group 2 (G2), composed by LA size between 43 and 46 mm; and Group 3 (G3), composed by LA size between 47 and 55 mm. Figure 3 shows the different curves of AF recurrence, according to LA size, considering all procedures.

Table 4 depicts the AF recurrence according to LA size.

The area under the ROC curve of LA size to predict AF recurrence was 0.89 (95% CI: 0.812-0.968).

Safety of the procedure

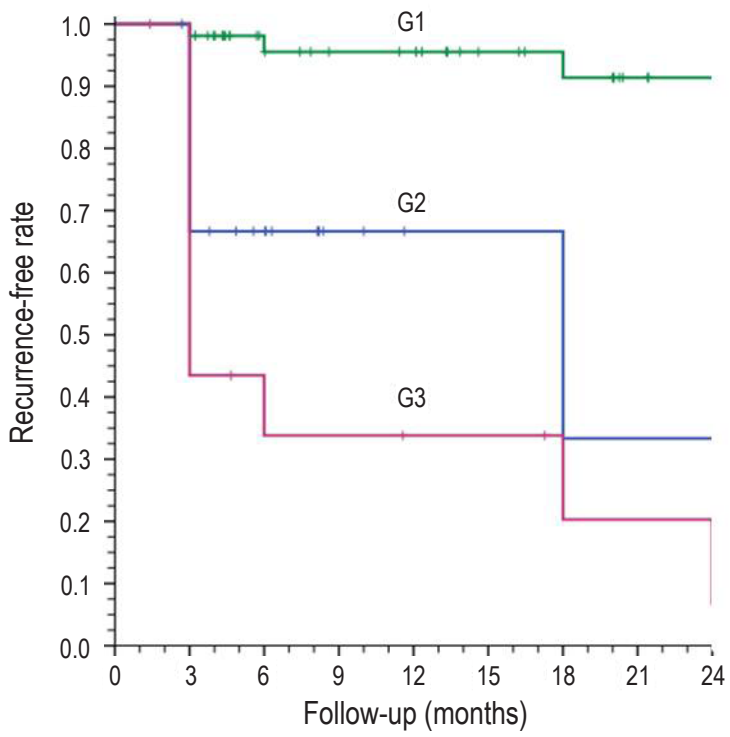
There were five complications related to the procedure (4.9%). One patient evolved with EVA, and the thrombus was visualized on intracardiac echocardiogram after transseptal puncture; however, the thrombus detached before it could be aspirated. The procedure was suspended. After recovering from anesthesia, the patient had clinical signs of EVA with a National Institutes of Health (NIH) Stroke Scale of 11[10]. That finding was confirmed on magnetic resonance. The patient was successfully treated with alteplase two hours after symptom onset (NIH = 0, 8 hours after end of infusion).

One patient with PV stenosis diagnosed on computed tomographic angiography was followed up. Because of the low repercussion on scintigraphy, clinical treatment was chosen. Another complication was the formation of a pseudoaneurysm in the femoral region, which was surgically fixed. Two patients had similar cases of pulmonary edema with normal pulmonary capillary pressure associated with an important increase in inflammation markers (erythrocyte sedimentation rate and C-reactive protein) 24 hours after extensive ablations, due to long-standing persistent AF. Both patients responded to high corticosteroid doses, with a satisfactory outcome after 48 hours. A 70-year-old male patient, with creatinine clearance of 35 mL/min, died late (after 30 days), due to a cause not related to the procedure, but to a hemorrhagic EVA secondary to anticoagulant therapy.

Discussion

Radiofrequency catheter ablation has undergone rapid development, being currently one of the major therapeutic options for the treatment of AF[8].

With the accumulation of evidence regarding the efficacy and safety of the procedure, in 2012 a new recommendation was suggested by the HRS/EHRA/ESC expert consensus, classifying RF catheter ablation as class I, level of evidence A, for symptomatic patients with paroxysmal AF refractory to drug therapy. The same document published a consensus about the technical aspects and the strategies used for the AF ablation treatment. Regardless of the technique used, the complete electrical isolation of all PV should be performed as the initial objective of the procedure[4]. The tridimensional mapping provides better accuracy to identify the anatomy for RF application on the LA and around the PV[6].



Procedures (n)	G1	53	52	38	33	32	25	23	17	19
	G2	25	23	13	6	4	4	4	1	1
	G3	24	22	9	7	6	6	5	3	2
Recurrence-free rate (%)	G1	100.0	98.1	**95,5**	95.5	95.5	95.5	91.4	91.4	91.4
	G2	100.0	66.1	**66,7**	66.7	66.7	66.7	33.3	33.3	33.3
	G3	100.0	43.5	**33,8**	33.8	33.8	33.8	20.3	20.3	20.3

Figure 3 - *Kaplan-Meier curve for atrial fibrillation recurrence after the procedure, according to left atrium size.*

Table 4 - Atrial fibrillation (AF) recurrence rate according to the left atrium (LA) size

LA size (mm)	n	AF recurrence n (%)	HR	95% CI	p value
34-42	53	3 (5,7)	-	-	-
43-46	25	10 (40,0)	10,04	1,51-66,77	0,017
47-55	24	20 (83,3)	18,07	2,71-120,58	0,003

*p value trend < 0.001; * Wald chi-square versus baseline group (normal left atrium range: 34-39 mm). HR: incidence density ratio; 95% CI: 95% confidence interval.*

Based on the recurrence rate, many patients are candidates to repeat ablation. Two systematic reviews and one meta-analysis involving patients with paroxysmal or persistent or long-standing persistent AF had a success rate of one single ablation of 57%, and that rate increased to 77% when considering multiple procedures[11].

In this study, the number of patients free from recurrence was higher among those with paroxysmal AF and persistent AF than among patients with long-standing persistent AF during follow-up.

An important factor to be considered was the possible influence of the learning curve[12]. There was a reduction in

the total procedure duration as well as in the radioscopy duration with the learning curve, the latter being also influenced by the association of reconstruction by use of the Cartomerge software. Such results were similar to those of the study by Tang et al[13] Nevertheless, the same findings have not been reported by the Italian registry[14].

Despite the greater number of AF recurrences after the initial procedures (54% within the first three years from the procedure), the post-procedure rate of AF recurrence-free patients was similar to that reported in the literature[15-19]. When analyzing only the last two years, the post-procedure rate of AF recurrence-free patients was 77%, similar to those of centers with a greater experience in that type of procedure, whose rates have ranged from 20% to 60%[20-22].

Enlargement of the LA was the only variable independently associated with AF recurrence after the procedure. In the Framingham Heart Study, LA enlargement was also considered an independent predictor of AF appearance in the general population[23]. Several studies have identified factors associated with post-ablation AF recurrence, and the LA size has been the most frequently found variable[24,25]. The study by Hsieh et al[24] has shown that, in 207 patients undergoing ablation, the major clinical variables found in patients with recurrence after one year were SAH and LA enlargement defined as a LA diameter > 40 mm. Such data are similar to those from the study by Berruezo et al[26], which identified LA enlargement as an independent predictor of AF recurrence after RF ablation. Recently, Zhuang et al[27] have reported a meta-analysis with 22 studies, including 3,750 patients, emphasizing that LA enlargement is an advanced marker of remodeling and the major marker of the increased risk for AF after ablation. Another meta-analysis, which is being prepared for publication, has shown that LA diameter > 50 mm was a predictor for AF recurrence[28]. This study showed a significant increase in the post-ablation recurrence associated with LA size. Left atrial enlargement is associated with a degree of atrial remodeling manifested as increased fibrosis, with changes in the substrate, favoring AF persistence[29] and hindering the efficacy of RF ablation because of the need for deeper lesions to complete ablation[30].

Among the complications observed, two cases of an inflammatory pulmonary syndrome[31,32] associated with procedures, in which additional lines in the LA posterior wall were performed, stand out. That complication has been clearly described neither in the literature nor in any world series of AF ablation. That finding is believed to be related to an inflammatory response to the extensive lesions performed in some procedures. However, a larger number of cases should be observed to better clarify that type of complication. The complication rate found in this study (4.9%) and related to the procedure was similar to that of the last world registry on AF ablation (4.5%)[33], but lower than that reported in the registry of the Brazilian Society of Cardiac Arrhythmias (14.5%)[19].

Study limitations

Important limitations should be considered when analyzing the results of this study. The major limitations are the learning curve for performing a complex procedure and the small number of recurrences, which is the major limitation in this study for identifying other independent variables associated with this outcome. The magnitude of the event has not been clearly determined due to the small size of the sample. Limitations associated with this type of analysis, such as asymptomatic recurrences, are inherent in studies on AF ablation[34,35] and should be considered.

Conclusions

The efficacy of RF catheter AF ablation guided by electroanatomical mapping found in this study was similar to that of other centers with experience in that type of procedure. The learning curve proved to be important in reducing the durations of the procedure and of radioscopy, and in the efficacy of AF ablation in this series.

In the present study, the size of the LA was the only variable with independent value for the AF recurrence outcome.

Author contributions

Conception and design of the research: Kalil C. Acquisition of data: Kalil C, Bartholomay E, Borges AP, Gazzoni G, Lima E, Etchepare R, Moraes R, Sussenbach C, Andrade K. Analysis and interpretation of the data: Kalil C, Bartholomay E. Statistical analysis: Kalil C. Writing of the manuscript: Kalil C, Bartholomay E, Borges AP. Critical revision of the manuscript for intellectual content: Kalil C, Kalil R. Supervision / as the major investigator: Kalil R.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

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Study Association

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References

1. Camm AJ, Llp GY, De Caterina R, Savelioeva I, Atar D, Hohnloser S, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation – an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J. 2012;33(21):2719-47. Erratum in Eur Heart J. 2013;34(10):790.

2. Zimerman LI, Fenelon G, Martinelli Filho M, Grupi C, Atié J, Lorga Filho A, et al; Sociedade Brasileira de Cardiologia. Diretrizes brasileiras de fibrilação atrial. Arq Bras Cardiol. 2009;92(6 supl.1):1-39.

3. Fuster V, Ryden LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, et al; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; European Society of Cardiology Committee for Practice Guidelines; Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation-executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). J Am Coll Cardiol. 2006;48(4):854-906. Erratum in: J Am Coll Cardiol. 2007;50(6):562.

4. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society. Heart Rhythm. 2012;9:632-696 e621.

5. Haïssaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med. 1998;339(10):659-66.

6. Pappone C, Oreto G, Rosanio S, Vicedomini G, Tocchi M, Gugliotta F, et al. Atrial electroanatomic remodeling after circumferential radiofrequency pulmonary vein ablation: efficacy of an anatomic approach in a large cohort of patients with atrial fibrillation. Circulation. 2001;104(21):2539-44.

7. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savalieva I, Ernst S, et al; European Heart Rhythm Association; European Association for Cardio-Thoracic Surgery. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J. 2010;31(19):2369-429. Erratum in: Eur Heart J. 2011;32(9):1172.

8. Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJ, et al; European Heart Rhythm Association (EHRA); European Cardiac Arrhythmia Society (ECAS); American College of Cardiology (ACC); American Heart Association (AHA); Society of Thoracic Surgeons (STS). HRS/EHRA/ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on catheter and surgical ablation of atrial fibrillation. Heart Rhythm. 2007;4(6):816-61. Erratum in: Heart Rhythm. 2009;6(1):148.

9. Kirchhof P, Auricchio A, Bax J, Crijns H, Camm J, Diener HC, et al.Outcome parameters for trials in atrial fibrillation: executive summary. Eur Heart J. 2007;28(22):2803-17.

10. Lyden P, Lu M, Jackson C, Marler J, Kothari R, Brott T, et al. Underlying structure of the National Institutes of Health Stroke Scale: results of a factor analysis. NINDS tPA Stroke Trial Investigators. Stroke. 1999;30(11):2347-54.

11. Calkins H, Reynolds MR, Spector P, Sondhi M, Xu Y, Martin A, et al. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. Circ Arrhythm Electrophysiol. 2009;2(4):349-61.

12. Naccarelli GV, Conti JB, DiMarco JP, Tracy CM; Heart Rhythm Society. Task force 6: training in specialized electrophysiology, cardiac pacing, and arrhythmia management endorsed by the Heart Rhythm Society. J Am Coll Cardiol. 2008;51(3):374-80.

13. Tang K, Ma J, Zhang S, Zhang JY, Wei YD, Chen YQ, et al. A randomized prospective comparison of CartoMerge and CartoXP to guide circumferential pulmonary vein isolation for the treatment of paroxysmal atrial fibrillation. Chin Med J (Engl). 2008;121(6):508-12.

14. Bertaglia E, Bella PD, Tondo C, Proclemer A, Bottoni N, De Ponti R, et al. Image integration increases efficacy of paroxysmal atrial fibrillation catheter ablation: results from the CartoMerge Italian Registry. Europace. 2009;11(8):1004-10.

15. Cappato R, Calkins H, Chen SA, Davies W, Ieseka Y, Kalman J, et al. Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. J Am Coll Cardiol. 2009;53(19):1798-803.

16. Pappone C, Augello G, Sala S, Gugliotta F, Vicedomini G, Gulletta S, et al. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal atrial fibrillation: the APAF Study. J Am Coll Cardiol. 2006;48(11):2340-7.

17. Jais P, Cauchemez B, Macle L, Daoud E, Khairy P, Subbiah R, et al. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. Circulation. 2008;118(24):2498-505. Erratum in Circulation. 2009 Sep 8;120(10):e83

18. Wazni OM, Marrouche NF, Martin DO, Verma A, Bhargava M, Saliba W, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. JAMA. 2005;293(21):2634-40.

19. Fenelon G, Scanavacca M, Atié J, Zimerman L, Magalhães LP, Larga Filho A, et al. Ablação da fibrilação atrial no Brasil: resultados do registro da Sociedade Brasileira de Arritmias Cardíacas. Arq Bras Cardiol. 2007;89(5):258-62, 285-9.

20. Karch MR, Zrenner B, Deisenhofer I, Schreieck J, Ndrepepa G, Dong J, et al. Freedom from atrial tachyarrhythmias after catheter ablation of atrial fibrillation: a randomized comparison between 2 current ablation strategies. Circulation. 2005;111(22):2875-80.

21. Pappone C, Manguso F, Vicedomini G, Gugliotta F, Santinelli O, Ferro A, et al. Prevention of iatrogenic atrial tachycardia after ablation of atrial fibrillation: a prospective randomized study comparing circumferential pulmonary vein ablation with a modified approach. Circulation. 2004;110(19):3036-42.

22. Oral H, Scharf C, Chugh A, Hall B, Cheung P, Good E, et al. Catheter ablation for paroxysmal atrial fibrillation: segmental pulmonary vein ostial ablation versus left atrial ablation. Circulation. 2003;108(19):2355-60.

23. Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic atrial fibrillation. The Framingham Heart Study. Circulation. 1994;89(2):724-30.

24. Hsieh MH, Tai CT, Tsai CF, Lin WS, Lin YK, Tsao HM, et al. Clinical outcome of very late recurrence of atrial fibrillation after catheter ablation of paroxysmal atrial fibrillation. J Cardiovasc Electrophysiol. 2003;14(6):598-601.

25. Khankirawatana B, Khankirawatana S, Porter T. How should left atrial size be reported? Comparative assessment with use of multiple echocardiographic methods. Am Heart J. 2004;147(2):369-74.

26. Berruezo A, Tamborero D, Mont L, Benito B, Tolosana JM, Sitges M, et al. Pre-procedural predictors of atrial fibrillation recurrence after circumferential pulmonary vein ablation. Eur Heart J. 2007;28(7):836-41.

27. Zhuang J, Wang Y, Tang K, Li X, Peng W, Liang C, et al. Association between left atrial size and atrial fibrillation recurrence after single circumferential pulmonary vein isolation: a systematic review and meta-analysis of observational studies. Europace. 2012;14(5):638-45.

28. D'Ascenzo F, Corleto A, Biondi-Zoocai G, Anselmino M, Ferraris F, di Biase L, et al. Which are the most reliable predictors of recurrence of atrial fibrillation after transcatheter ablation?: a meta-analysis. Int J Cardiol 2012 May 22. [Epub ahead of print].

29. Burstein B, Nattel S. Atrial fibrosis: mechanisms and clinical relevance in atrial fibrillation. J Am Coll Cardiol. 2008;51(8):802-9.

30. Oakes RS, Badger TJ, Kholmovski EG, Akoum N, Burgon NS, Fish EN, et al. Detection and quantification of left atrial structural remodeling with delayed-enhancement magnetic resonance imaging in patients with atrial fibrillation. Circulation. 2009;119(13):1758-67.

31. Suh GY, Kang EH, Chung MP, Lee KS, Han J, Kitaichi M, et al. Early intervention can improve clinical outcome of acute interstitial pneumonia. Chest. 2006;129(3):753-61.

32. Johkoh T, Muller NL, Taniguchi H, Kondoh Y, Akira M, Ichikado K, et al. Acute interstitial pneumonia: thin-section CT findings in 36 patients. Radiology. 1999;211(3):859-63.

33. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. Circ Arrhythm Electrophysiol. 2010;3(1):32-8.

34. Hindricks G, Piorkowski C, Tanner H, Kobza R, Gerds-Li JH, Carbucicchio C, et al. Perception of atrial fibrillation before and after radiofrequency catheter ablation: relevance of asymptomatic arrhythmia recurrence. Circulation. 2005;112(3):307-13.

35. Neumann T, Erdogan A, Dill T, Greiss H, Berkowitsch A, Sperzel J, et al. Asymptomatic recurrences of atrial fibrillation after pulmonary vein isolation. Europace. 2006;8(7):495-8.