ORIGINAL ARTICLE

Predictors of Recurrence and Outcomes in Catheter Ablation of Paroxysmal Atrial Fibrillation

Predictores de recurrencia y resultados en la ablación de la fibrilación auricular paroxística

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ABSTRACT

Background: Pulmonary vein isolation is currently the treatment of choice in patients with symptomatic paroxysmal atrial fibrillation refractory to antiarrhythmic therapy. Different groups specialized in treating paroxysmal atrial fibrillation have published their experience and many predictors of recurrence have been identified. However, so far, a similar experience has not been reported in our environment.
Objectives: The primary endpoint was to analyze the predictors of recurrence after pulmonary vein isolation with radiofrequency catheter ablation. The secondary endpoint was to evaluate the success rate and procedure-related complications.
Methods: A retrospective, observational and single-center study was conducted between May 2009 and August 2015 on 1,000 consecutive cases of radiofrequency catheter ablation procedures for paroxysmal atrial fibrillation guided by electroanatomical mapping. A total of 507 pulmonary vein isolation procedures with at least 1-year follow-up were analyzed, excluding repeat ablation procedures and patients who did not complete all follow-up visits.
Results: A multivariate analysis using the Cox regression model showed that the higher rate of episodes of atrial fibrillation before ablation [HR 1.354 (1.059-1.732); p = 0.016] and early recurrence (0-3 months) [HR 4.006 (2.703-5.937); p < 0.0001] were the most significant predictors of recurrence at 12 months.
The rate of sinus rhythm maintenance at one year without antiarrhythmic treatment was 77.5% for paroxysmal atrial fibrillation, with a recurrence of 22.5%.
The complications included cardiac tamponade requiring pericardiocentesis in 16 patients (1.6%), vascular complications in 21 (2.1%), transient ischemic attack in 2 (0.2%), phrenic nerve palsy in 1 (0.1%), pericarditis in 5 (0.5%) and hemothorax in 1 (0.1%).
Conclusions: Higher frequency of episodes of atrial fibrillation before pulmonary vein isolation and early recurrence are strong predictors of recurrence at one year.
Pulmonary vein isolation is a safe and effective method for rhythm control in patients with symptomatic paroxysmal atrial fibrillation refractory to antiarrhythmic therapy, with a low rate of complications.

Key words: Atrial Fibrillation - Pulmonary Veins - Ablation Techniques - Electrophysiologic Techniques, Cardiac

RESUMEN

Introducción: El aislamiento de las venas pulmonares es actualmente la terapéutica de elección en pacientes con fibrilación auricular paroxística, sintomática y refractaria al tratamiento antiarrítmico. Diferentes grupos abocados al tratamiento de la fibrilación auricular paroxística han publicado su experiencia y se conocen varios predictores de recurrencia. Sin embargo, hasta el presente no se ha reportado en nuestro medio una experiencia similar.
Objetivos: Primario: Analizar los predictores de recurrencia posaislamiento de venas pulmonares con radiofrecuencia. Secundario: Evaluar la tasa de éxito y las complicaciones asociadas con el procedimiento.
Material y métodos: Análisis prospectivo, observacional, unicéntrico, realizado entre mayo de 2009 y agosto de 2015 de 1.000 casos consecutivos de ablación de fibrilación auricular paroxística con radiofrecuencia y mapeo electroanatómico.
Para el análisis del seguimiento se utilizaron 507 aislamientos de venas pulmonares con al menos un año de seguimiento, excluyendo las reablaciones y los pacientes que no cumplieron con todas las visitas de seguimiento.
Resultados: En un análisis multivariado utilizando regresión de Cox se observó que la mayor frecuencia de episodios de fibrilación auricular previos a la ablación [HR 1,354 (1,059-1,732); p = 0,016] y la recurrencia temprana (0-3 meses) [HR 4,006 (2,703-5,937); p < 0,0001] fueron los predictores más significativos de recurrencia a los 12 meses.
La tasa de mantenimiento de ritmo sinusal al año sin tratamiento antiarrítmico fue del 77,5% para fibrilación auricular paroxística, con una recurrencia del 22,5%.
Las complicaciones fueron taponamiento cardíaco con pericardiocentesis en 16 pacientes (1,6%), complicaciones vasculares en 21

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(2,1%), ataque isquémico transitorio en 2 (0,2%), parálisis del nervio frénico en 1 (0,1%), pericarditis en 5 (0,5%) y hemotórax en 1 (0,1%).
Conclusiones: La mayor frecuencia de episodios de fibrilación auricular previos al aislamiento de venas pulmonares y la recurrencia temprana favorecen la recurrencia al año.
El aislamiento de venas pulmonares es un método seguro y eficaz para el control del ritmo en pacientes con fibrilación auricular paroxística, sintomática y refractaria al tratamiento antiarrítmico, con una tasa baja de complicaciones.

Palabras clave: Fibrilación auricular - Venas pulmonares - Técnicas de ablación - Técnicas electrofisiológicas cardíacas

Abbreviations

LA	Left atrium	**aPTT**	Activated partial thromboplastin time
PVI	Pulmonary vein isolation	**INR**	International normalized ratio
AF	Atrial fibrillation	**CMRI**	Cardiac magnetic resonance imaging
PAF	Paroxysmal atrial fibrillation	**ACT**	Activated clotting time
LVEF	Left ventricular ejection fraction	**64-MDCT**	64-detector row computed tomography
LMWH	Low-molecular-weight heparin		

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained arrhythmia, and probably the first to be recognized. Atrial fibrillation was first described by William Harvey in 1628 when he perceived dissociation between the peripheral pulse and the heartbeat. At the beginning of the 20th century (1902) Willem Einthoven, from the Netherlands, invented the electrocardiogram (ECG) and recorded 26 strips of various cardiac rhythm disturbances, one of which was AF, which he called pulsus inequalis and irregularis.

Throughout history, multiple theories have emerged about the origin of AF until the concept of re-entry was introduced by Winterberg in 1906. In 1912, Lewis proposed that AF was caused by multiple electrical foci. However, none of these theories was followed until the sixties, when the theory of multiple wavelets aroused interest and in the eighties, Allesie et al. (1) demonstrated the characteristics of the leading re-entry circuit that maintained the arrhythmia. More recently, in 1998 (2) Haïssaguerre contributed to one of the great progresses in the treatment of this arrhythmia by demonstrating the focal origin of paroxysmal atrial fibrillation (PAF) mostly in the pulmonary veins.

Atrial fibrillation affects 1-2% of the population and this percentage is expected to increase in the next 50 years. (3, 4) Recent studies have documented a prevalence <0.5% in subjects <50 years to 5-15% or greater in subjects >80 years. (5) Although AF is more common in men, with age the prevalence is similar in men and women.

Atrial fibrillation is associated with increased mortality, (6) with a 5-fold increased risk of stroke (7) and a 3-fold increase in the risk of heart failure and hospitalizations. (8) It also impairs quality of life and left ventricular dysfunction and reduces exercise capacity. (9)

Pulmonary vein isolation (PVI) by radiofrequency catheter ablation is a well-established treatment in patients with symptomatic or refractory PAF or in patients intolerant to antiarrhythmic therapy, and the number of procedures has constantly increased over the past decade. (10-12)

Different groups have published their experience in the treatment of AF, and even a worldwide database has been created to report the results and limitations of this treatment. (13) However, so far, a similar experience has not been reported in our setting.

This study describes the results of PVI using radiofrequency catheter ablation for PAF treatment, analyzing the clinical characteristics of the patients, the predictors of long-term recurrence after PVI, the rate of success and procedure-related complications.

METHODS

A retrospective, observational, single-center study was conducted between May 2009 and August 2015 on 1,000 consecutive cases of radiofrequency catheter ablation for PAF guided by electroanatomical mapping (792 cases as a first procedure and 208 as a repeat ablation).

Follow-up at 1, 2, 3, 6, 9 and 12 months included ECG and 24-hour Holter monitoring.

A total of 507 PVIs for PAF with at least 1-year follow-up were analyzed, excluding repeat ablation procedures and patients who did not complete all follow-up visits.

All the information was obtained from our institutional Microsoft Access database.

Anticoagulation strategy

Patients with a CHA_2DS_2VASc score ≥1 received oral anticoagulants for at least three weeks under monitoring of the therapeutic international normalized ratio (INR). When INR was <2.0, the anticoagulant was replaced by subcutaneous enoxaparin (1 mg/kg bid) before the procedure. In cases receiving new oral anticoagulants, only the last dose was stopped.

During the procedure and after transseptal puncture, an intravenous bolus of heparin sodium was administered (200 UI/kg) and activated clotting time (ACT) was monitored every 30 minutes until it was ≥350 seconds during all the procedure. Intravenous protamine was administered after the procedure to correct anticoagulation until the ACT reached ≤170 seconds in order to remove the intravascular introducers and sheaths. One hour after the procedure ended, intravenous heparin was administered by infusion pump

until aPTT reached 1.6 to 2.3 times the baseline value. The following morning, subcutaneous low-molecular-weight-heparin (LMWH) and the oral anticoagulant were administered. In the case of new oral anticoagulants, LMWH was not administered.

Catheter ablation procedure

All the procedures were performed under general anesthesia with routine monitoring of invasive arterial pressure, digital pulse oximetry and intraesophageal temperature.

All the patients underwent a 64-detector row computed tomography (64-MDCT) scan or cardiac magnetic resonance imaging (CMRI) in case of contraindications.

Transesophageal echocardiography was performed on the same day of the procedure only if the levels of anticoagulation were inconsistent to exclude left atrial (LA) thrombi or to guide difficult transseptal punctures.

A 12-lead electrocardiogram (ECG) and intracardiac bipolar electrograms were recorded using electronic calibrators (EP-WorkMate 4.2 System, St. Jude Medical, Inc) at a screen speed of 50 to 200 mm/s and were filtered at band-pass settings of 50 to 500 Hz.

A non-fluoroscopic mapping navigation system was used in all cases (Ensite™ Velocity™ cardiac mapping system, St. Jude Medical Inc.).

After both femoral veins were punctured, a decapolar catheter was placed in the coronary sinus. Under radioscopic guidance, two transseptal punctures in the 40° left anterior oblique projection, were performed with Brockenbrough needle; then, two long SL1 and SL2 preshaped introducers (St. Jude Medical Inc.) were positioned. An Optima Plus circular duo-decapolar catheter and a Therapy-Cool™ irrigated-tip ablation catheter (St. Jude Medical Inc.) were advanced through the introducers to deliver radiofrequency. The anatomical reconstruction was performed using the circular Optima Plus mapping catheter which is capable of simultaneous recording from multiple points and the ablation catheter was used to identify the ostium and the antrum of the pulmonary veins.

The electric activity of each pulmonary vein was obtained using the circular catheter. Pulmonary vein isolation started in the left superior pulmonary vein and continued in the left inferior pulmonary vein. The same sequence was used for the right pulmonary veins. Radiofrequency energy was delivered at the anterior and posterior aspect of each pulmonary vein with a power output of 40 W and 35 W, respectively. The lesions were applied to the antrum but not the ostium of the veins. The electrograms recorded by the ablation catheter before and after applying the ablation lesion were analyzed in each patient. The target was a reduction of the potential amplitude by at least 75% and the elimination or dissociation between atrial activity and pulmonary vein activity. Once the isolation was completed, the presence of persistent block in each pulmonary vein was evaluated. If necessary, ablation was repeated to consolidate the line of bidirectional block.

All the methods available were used to discriminate local or remote electrical activity.

Patients underwent neurological examination after recovery from anesthesia at the electrophysiology laboratory and before discharge.

Definition of complications

All the complications were documented by a staff physician of the electrophysiology laboratory and were entered in our database.

Major complications were defined as those producing a permanent sequel and/or death, extending hospital stay >48 hours or requiring rehospitalization.

Postoperative care

All the patents were transferred to the intensive care unit with central monitoring. Transthoracic echocardiography was performed to all the patients to exclude pericardial effusion or other detectable complications. Oral anticoagulation and antiarrhythmic therapy was started at discharge.

Follow-up

Follow-up visits were systematically scheduled at 1, 2, 3, 6, 9 and 12 months. During each visit, the patients were interrogated about symptoms suggestive of arrhythmia or related with the procedure and the results of 24-hour Holter monitoring and 12-lead ECG were analyzed. Patients were encouraged to pick up the 12-lead ECG record and seek medical advice in the emergency department in case of signs suggestive of AF. In case of recurrent AF after the 3-month blanking period or before if the clinical condition was determinant, a second ablation procedure was suggested. Oral anticoagulation was generally stopped in patients without recurrences or other indications of anticoagulation, as prosthetic heart valves, $CHA_2DS_2VASC \geq 1$ or thromboembolic events. The same occurred with antiarrhythmic treatment. Atrial tachycardia and atrial flutter originated in the left atrium were classified as failed ablation due to arrhythmia recurrence. Recurrent AF was defined as the presence of episodes of AF/atrial tachycardia or atrial flutter originated in the left atrium lasting for >30 seconds and documented by Holter monitoring, ECG or central monitoring.

Statistical analysis

Discrete variables are expressed as percentages and continuous variables as mean and standard deviation.

The Cox proportional hazard model was used to evaluate predictors of recurrence after PVI.

Event-free survival was estimated using the Kaplan-Meier method and was compared with the log-rank test.

All the calculations were obtained using IBM SSPS Statistics 20 software.

Ethical considerations

The study protocol was evaluated and approved by the institutional Ethics Committee. An informed consent was not required due to the retrospective nature of the study (Law 3101, CABA).

RESULTS

The general characteristics of the population are presented in Table 1.

In the population, 75.2 % were men, 49.5% had hypertension, 4.4% were diabetic, LVEF was 61.27 ± 6% and LA area was 22.3 ± 4.5 cm2. Mean CHA_2DS_2-VASc score was 1.12 ± 1.1. Nineteen percent of the patients underwent catheter ablation as first-line therapy for different reasons, as high performance sports athletes, intolerance to antiarrhythmic therapy or patient's preference.

The rate of sinus rhythm maintenance at one year without antiarrhythmic treatment was 77.5% for PAF with a recurrence of 22.5%.

Among the 507 patients who completed follow-up, multivariate analysis using the Cox regression model showed that the number of episodes before ablation [HR 1.354 (95% CI 1.059-1.732); p = 0.016] and early recurrence (0-3 months) [HR 4.006 (95% CI 2.703-5.937); p <0.0001] were the most significant predictors of recurrence at 12 months (Table 2).

Complications occurred in 46 (4.6%) of the 1,000 ablation procedures performed, including cardiac tamponade requiring pericardiocentesis in 16 (1.6%), vascular complications in 21 (2.1%), transient ischemic attack (TIA) in 2 (0.2%) and phrenic nerve palsy in 1 (0.1%) (Table 3). None of the patients presented atrioesophageal fistula, symptomatic pulmonary vein stenosis or procedure-related mortality.

DISCUSSION

Catheter ablation for AF has become the treatment of choice in symptomatic patients, refractory AF or in those intolerant to antiarrhythmic therapy. (14, 15)

Several authors have published their experiences (16-18) and results over the past 10 years. Even a worldwide database regularly reports the overall success rates. (12) However, knowing the local reality may be one of the main determinants at the moment of indicating this type of major procedure.

This is the first report about the outcomes and follow-up at 1 year of 1,000 catheter ablation procedures for PAF in a high-volume center (19) in Argentina.

The results reported in this study indicate that AF ablation is a good strategy for rhythm control, achieving a success rate of 77.5% with the first procedure. These results are consistent with other experiences worldwide. (20) The incidence of early recurrence was a strong predictor of recurrence at 1 year, producing a 4-fold increase in the risk of recurrence. Therefore, reducing early recurrence after ablation could increase the rate of freedom from AF within the first year after ablation (Figure 1). The pathophysiology of recurrence in this period might not be determined by the inflammation generated by the lesion, as the recurrence is still high once inflammation is overcome, but probably by the level of transmural extent of the lesion. The correlation with the findings at the moment of a second ablation procedure and the use of new technologies (21) could make a significant change in the outcome of patients undergoing this treatment. This theory could be confirmed by new studies and analyses.

The number of episodes of AF before PVI was another predictor of late recurrence in our study. This variable is a piece of clinical information available to all the professionals taking care of patients with AF. This concept makes us think that the process of left atrial electrical remodelling is accelerated in patients with higher number of AF episodes. These patients could benefit from an earlier ablation strategy to improve the results of this technique and increase the long-term success rate. (22, 23)

Several authors have found other predictors of recurrence as age, sex, left atrial area or left ventricular ejection fraction (LVEF). None of these variables predicted recurrence in our series. A possible reason

Table 1. Population characteristics

Age, years	62.2±11
Male sex, %	75.2
Diabetes, %	4.4
Hypertension, %	49.5
LVEF, %	61.27±6
LA area, cm2	22.31±4.5
CHA_2DS_2-VASc	1.12±1.1
Early recurrence, %	14.7
Recurrence at 1 year, %	22.5

LVEF: Left ventricular ejection fraction. LA: Left atrium.

Table 2. Univariate and multivariate analysis of atrial fibrillation recurrence predictors at 1 year after pulmonary vein isolation using the Cox regression model.

Variable	Univariate analysis		Multivariate analysis	
	HR	p	HR	p
Sex	1.195 (0.767-1.861)	0.432	1.177 (0.750-1.848)	0.478
Age	0.989 (0.974-1.005)	0.173	0.998 (0.981-1.015)	0.806
LVEF <45%	1.582 (0.646-3.876)	0.316	-	ns
Frequency of episodes				
>1 x week				
<1 x week, >1 x month				
<1 x month, >1 every 6 months	1.489 (1.170-1.895)	0.001	1.354 (1.059-1.732)	0.016
LA >24 cm2	1.218 (0.827-1.793)	0.318	-	ns
Early recurrence	4.298 (2.991-6.323)	<0.0001	4.006 (2.703-5.937)	<0.0001

LVEF: Left ventricular ejection fraction. LA: Left atrium. ns: Non-significant.

for these findings could be explained by the characteristics of the population undergoing radiofrequency catheter ablation in our institution where the percentage of comorbidities is low. In addition, the use a cutoff point of 24 cm2 for left atrial area and 45% for LVEF in a population with low comorbidities would not discriminate AF secondary to left atrial dilation.

The rate of complications was 4.6%, with a low incidence of potentially lethal complications as cardiac tamponade (1.6%), TIA (0.2%) and phrenic nerve palsy (0.1%). Vascular complications were the most prevalent adverse events. The role of LMWH has not been determined yet, (24) and continuous anticoagulation seems to be a safe strategy. (25, 26) The use of vascular ultrasound during the procedure is another measure that might contribute to reduce this type of complication. Transient ischemic attacks occurred in two patients who were not receiving intravenous anticoagulants in the postoperative period because of hemorrhagic complications, not allowing adequate inhibition of the coagulation cascade activation due to endothelial disruption.

The rate of cardiac tamponade in this study was slightly greater than the one published in other series. This finding could be attributed to the fact that we did not use intracardiac echocardiography, (27) (a tool that has been recently incorporated to our institution), and to the lack of ablation catheters with contact force sensors (28) which could prevent the occurrence of this complication according to the literature available. (29) We did not find sudden impedance changes or audible boops suggesting tissue overheating in any of the cases as reported by other authors. (30)

Finally, the level of complications is consistent with those reported by high-volume centers and lower than those reported by other series in Latin America and Europe. (20, 31)

We think that the experience of the center with over 200 cases of AF ablation procedures per year and the small number of operators are the factors most significantly associated with the low incidence of complications and the high success rate.

All the complications developed in 46 patients were resolved with treatment and without sequels. There were no cases of symptomatic pulmonary vein stenosis, atrioesophageal fistula or procedure-related mortality.

Table 3. Major complications, type and frequency

Type of complication	n	%
Cardiac tamponade	16	16
Pericarditis	5	5
TIA	2	2
Phrenic nerve palsy	1	1
Vascular complications		
Arteriovenous fistula	3	3
Pseudoaneurysm	8	8
Bleeding at the femoral puncture site	10	10
Hemothorax	1	1
Total	46	46

Transient ischemic attack.

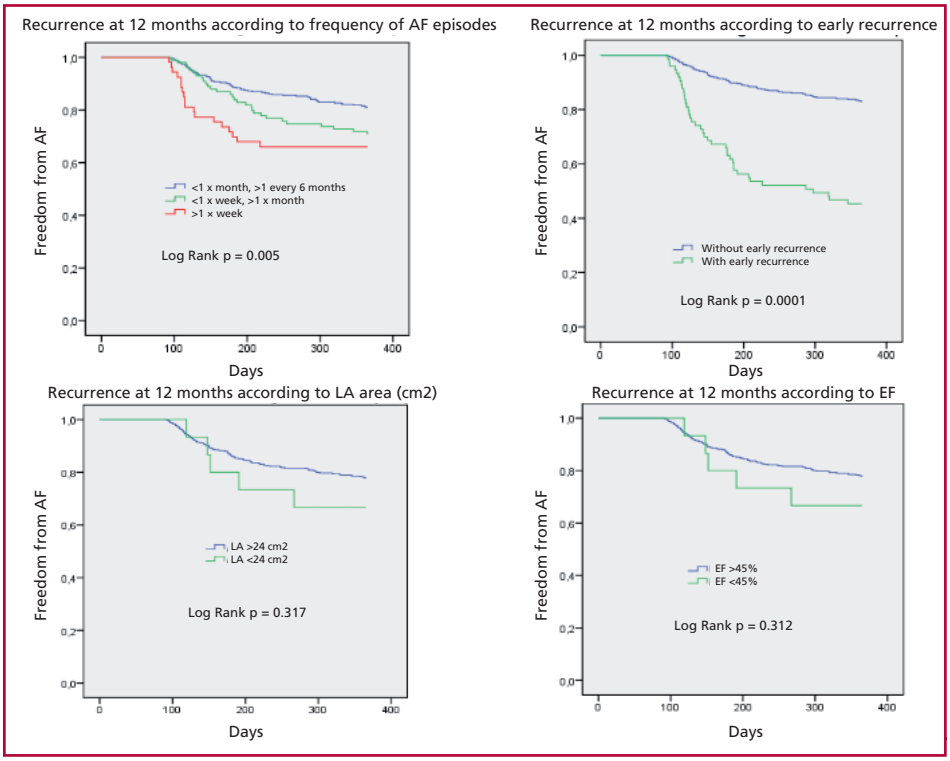

Fig. 1. Kaplan-Meier curves of recurrence predictors at 12 months after pulmonary vein isolation. A. The higher frequency of atrial fibrillation (AF) episodes before pulmonary vein isolation is associated with late recurrence. B. Early recurence is a strong predictor of late recurrence. C. Left atrium (LA) >24 cm2 did not predict late recurrence. D. Ejection fraction (EF) <45% was not associated with higher late recurrence.

Study limitations

This study has several potential limitations.

Only 76.14% of the patients completed all the Holter monitoring tests during follow-up, a limitation which may underestimate the rate of recurrence.

Many patients continued their follow-up in other cities of the country or neighboring countries and telephone contact was not possible. This limitation could underestimate the rate of recurrence as we do not know if they underwent strict controls.

Although we recorded the complications in our database, those occurring after discharge could have been lost.

Neither CMRI nor 64-MDCT scan are ordered as routine studies during follow-up, except for symptomatic patients or those undergoing a second ablation procedure; thus, the incidence of asymptomatic pulmonary vein stenosis could have been underestimated.

CONCLUSIONS

Pulmonary vein isolation is a good method for rhythm control in patients with symptomatic PAF, refractory AF or in those intolerant to antiarrhythmic therapy. Higher frequency of AF episodes before PVI and early recurrence are strong predictors of recurrence at one year.

The low rate of complications makes this technique a safe and efficient procedure for PAF treatment.

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Conflicts of interest

None declared. (See authors' conflicts of interest forms on the website/Supplementary material).

REFERENCES

1. Allessie MA, Bonke FI, Schopman FJ. Circus movement in rabbit atrial muscle as a mechanism of tachycardia: III. The "leading circle" concept. Circ Res 1977;41:9. http://doi.org/b8fk
2. 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;339:659-6. http://doi.org/bddjdv
3. Heerin J, van der Kuip DA, Hofman A, Kors JA, van Herpen G, Stricker BH, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J 2006;27:949-53. http://doi.org/cp3s7m
4. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. Arch Intern Med 1995;155:469-73. http://doi.org/fxch32
5. Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. Circulation 2006;114:119-25. http://doi.org/cs8qvt
6. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: The Framingham Heart Study. Circulation 1998;98:946-52. http://doi.org/45q
7. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The Framingham Study. Stroke 1991;22:983-8. http://doi.org/dhwbwv
8. Naccarelli GV, Hynes BJ, Wolbrette DH, Bhatta L, Khan M, Samii S, et al. Atrial fibrillation in heart failure. Prognostic significance and management. JCE 2003;14:281-6. http://doi.org/cgwj5p
9. Thrall G, Lane D, Carroll D, Lyp GY. Quality of life in patients with atrial fibrillation: a systematic review. Am J Med 2006;119:448.e1-448.e19. http://doi.org/dsz7zz
10. Wilber DJ, Pappone C, Neuzil P, DePaola A, Marchlinski F, Natale A, et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxismal atrial fibrillation: a randomized controlled trial. J Am Med Assoc 2010;303:333-40. http://doi.org/c8dw74
11. Oral H, Pappone C, Chugh A, Good E, Bogun F, Pelosi F Jr, et al. Circumferential pulmonary-vein ablation for chronic atrial fibrillation. N Engl J Med 2006;354:934-41. http://doi.org/cs6bp6
12. Packer DL, Kowal RC, Wheelan KR, Irwin JM, Irwin JM, Champagne J, et al. Cryoballoon ablation of pulmonary veins for paroxismal atrial fibrillation: first results of the North American Arctic Front (STOP AF) pivotal trial. J Am Coll Cardiol 2013;61:1713-23. http://doi.org/f2m68n
13. Cappato R, Calkins H, Chen SA, et al. Updated Worldwide Survey on the Methods, Efficacy, and Safety on Catheter Ablation for Human Atrial Fibrillation. Circulation Arrhythmia and Electrophysiology 2010;3:32-8. http://doi.org/fcn658
14. January C, Samuel W, Alpert J, Davies W, Iesaka Y, Kalman J, et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation. Circulation 2014;130:199-267. http://doi.org/9wb
15. Hadid C, Abello M, González JL. Consenso de Fibrilación Auricular. Sociedad Argentina de Cardiología. Rev Argent Cardiol 2015;83:1-22.
16. Scazzuso F, Rivera S, Sammartino V, Albina G, Laiño R, Giniger A. Pulmonary Vein Isolation for Treatment of Atrial Fibrillation. Rev Argent Cardiol 2012;80:21-6.
17. Haïssaguerre M, Jaïs P, Shah DC, Garrigue S, Takahashi A, Lavergne T, et al. Electrophysiological end point for catheter ablation of atrial fibrillation initiated from multiple pulmonary venous foci. Circulation 2000;101:1409-17. http://doi.org/sgm
18. Pappone C, Oreto G, Lamberti F, Vicedomini G, Loricchio ML, Shpun S, et al. Catheter ablation of paroxysmal atrial fibrillation using a 3D mapping system. Circulation 1999;100:1203-8. http://doi.org/b8fm
19. 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. Europace 2012;14:528-606. http://doi.org/b8fn
20. Keegan R, Aguinaga L, Fenelon G, Uribe W, Rodriguez Diez G, Scanavacca M, et al. The First Latin American Catheter Ablation Registry. Europace 2015;17:794-800. http://doi.org/f7ctwb
21. Kuck K, Reddy V, Schmidt B, Natale A, Neuzil P, Saoudi N, et al. A novel radiofrequency ablation catheter using contact force sensing: Toccata study. Heart Rhythm 2012;9:18-23. http://doi.org/b67r25
22. Nielsen JC, Johannessen A, Raatikainen P, Hindricks G, Walfridsson H, Kongstad O, et al. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation. N Engl J Med 2012;367:1587-95. http://doi.org/f2zrpz
23. Nielsen JC, Johannessen A, Raatikainen P, Hindricks G, Walfridsson H, Pehrson SM, et al. Long-term efficacy of catheter ablation as first-line therapy for paroxysmal atrial fibrillation: 5-year outcome in a randomised clinical trial. Heart 2016;26. http://doi.org/dg6w5j
24. Wazni OM, Beheiry S, Fahmy T, Barrett C, Hao S, Patel D, et al. Atrial fibrillation ablation in patients with therapeutic international normalized ratio: comparison of strategies of anticoagulation management in the periprocedural period. Circulation 2007;116:2531-4. http://doi.org/cb69k5
25. Di Biase L, Burkhardt JD, Mohanty P, Barrett C, Hao S, Patel D, et al. Periprocedural stroke and management of major bleeding complications in patients undergoing catheter ablation of atrial fibrillation: the impact of periprocedural therapeutic international normalized ratio. Circulation 2010;121:2550-6. http://doi.org/fzrhcg

26. Santangeli P, Di Biase L, Horton R, Burkhardt JD, Sanchez J, Al-Ahmad A, et al. Ablation of atrial fibrillation under therapeutic warfarin reduces periprocedural complications: evidence from a meta-analysis. Circ Arrhythm Electrophysiol 2012;5:302-11. http://doi.org/b9tqdb

27. Ren JF, Marchlinski FE. Utility of intracardiac echocardiography in left heart ablation for tachyarrthythmias. Echocardiography 2007;24:533-40. http://doi.org/f4cn28

28. Reddy V, Shah D, Kautzner J, Schmidt B, Saoudi N, Herrera C, et al. The relationship between contact force and clinical outcome during radiofrequency catheter ablation of atrial fibrillation in the TOCCATA study. Heart Rhythm 2012;9:1789-95. http://doi.org/f4cn28

29. Hsu LF, Jaïs P, Hocini M, Sanders P, Scavée C, Sacher F, et al. Incidence and prevention of cardiac tamponade complicating ablation for atrial fibrillation. Pacing Clin Electrophysiol 2005;28:106-9. http://doi.org/fjvsf9

30. Mourroche NF, Martin DO, Wazni O, Gillinov AM, Klein A, Bhargava M, et al. Phased array intracardiac echocardiography monitoring during pulmonary vein isolation in patients with atrial fibrillation: impact of outcome and complications. Circulation 2003;107:2710-6. http://doi.org/cx5533

31. Chen J, Dagres N, Hocini M, Fauchier L, Bongiorni MG, Defaye P, et al. Catheter ablation for atrial fibrillation: results from the first snapshot survey on procedural routine for atrial fibrillation ablation (ESS-PRAFA) part II. Europace 2015;17:1727-32. http://doi.org/f3nczp