Ablación de fibrilación auricular
¿A quién, cómo y cuándo?

XII Curso de fisiopatología cardiovascular.
CNIC. Noviembre-Diciembre 2018.

David Calvo Cuervo
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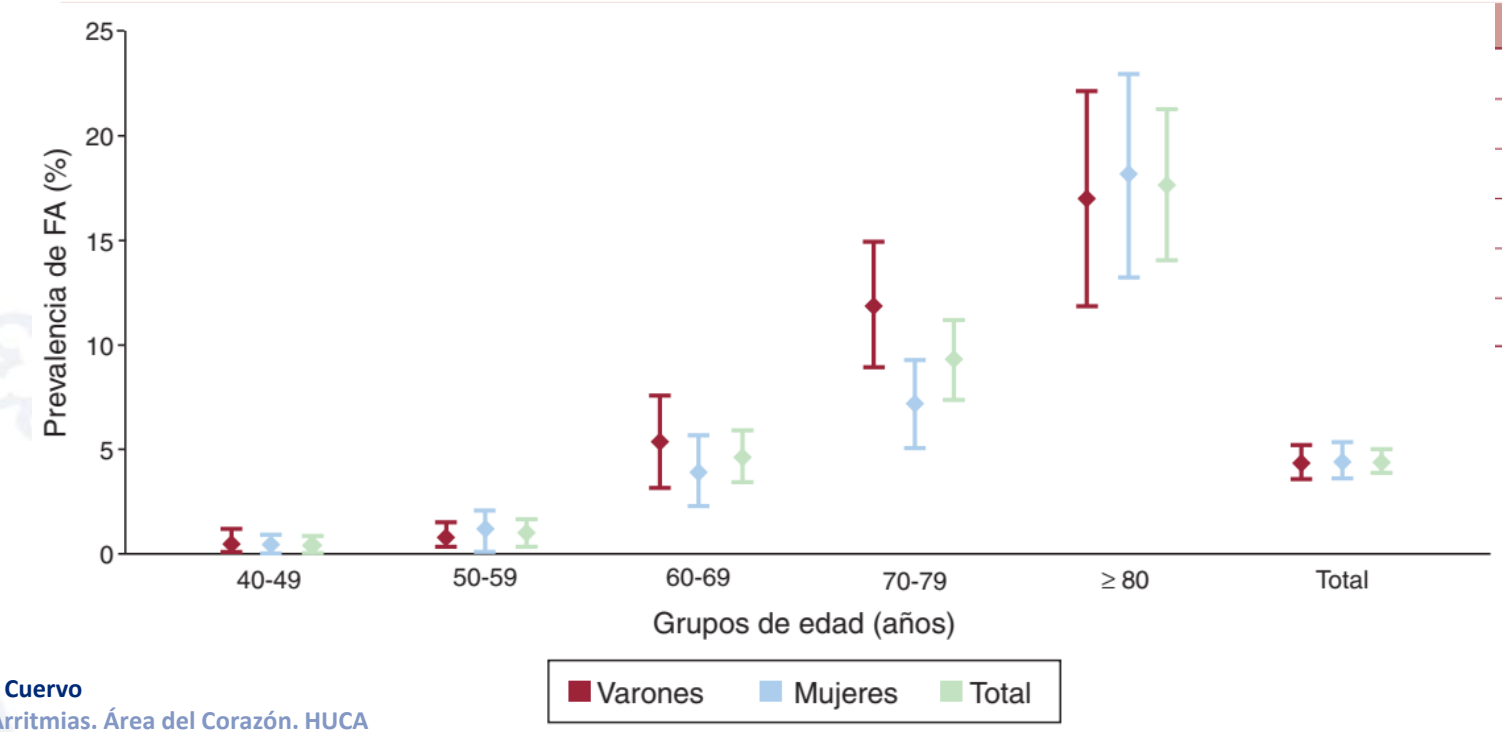
Hospital Universitario Central de Asturias. Spain

¿Cuál es la magnitud del problema? Prevalencia de FA.

	Varones (n = 3.829)		Mujeres (n = 4.514)		Total (n = 8.343)	
Edad	%	IC95%	%	IC95%	%	IC95%
40-49 años	0,5	0,0-1,2	0,2	0,0-0,4	0,3	0,0-0,7
50-59 años	0,9	0,3-1,6	1,1	0,1-2,1	1,0	0,4-1,7
60-69 años	5,3	3,1-7,5	4,0	2,3-5,7	4,6	3,4-5,9
70-79 años	11,9	8,9-14,9	7,2	5,1-9,3	9,3	7,4-11,2
≥ 80 años	17,0	11,9-22,1	18,1	13,3-22,9	17,7	14,1-21,3
Total	4,4	3,6-5,2	4,5	3,6-5,3	4,4	3,8-5,1

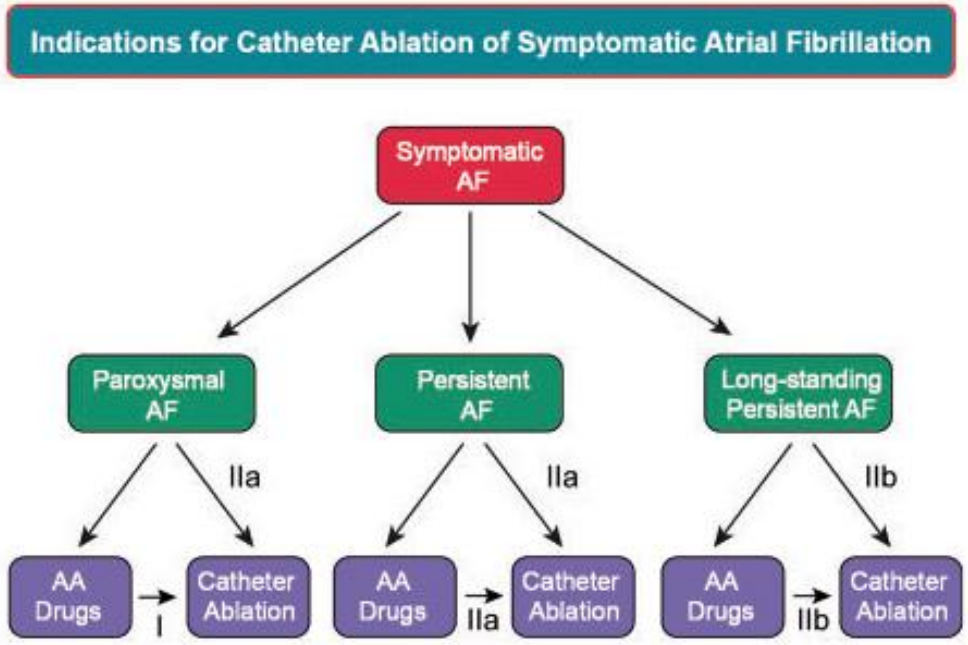


Total (en miles)	IC95%
23,6	0,0-50,9
58,3	21,4-95,2
207,4	145,3-269,4
321,8	252,9-390,9
414,7	326,2-503,3
1.025,8	879,1-1.172,6

Rev Esp Cardiol. 2014;67(4):259–269

¿Cuál es la magnitud del problema? Indicaciones de ablación de FA.

2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary



B. Indications for catheter atrial fibrillation ablation in populations of patients not well represented

Congestive heart failure	It is reasonable to use similar indications for AF ablation in selected patients with heart failure as in patients without heart failure.	IIa
Older patients (>75 years of age)	It is reasonable to use similar indications for AF ablation in selected older patients with AF as in younger patients.	IIa
Hypertrophic cardiomyopathy	It is reasonable to use similar indications for AF ablation in selected patients with HCM as in patients without HCM.	IIa
Young patients (<45 years of age)	It is reasonable to use similar indications for AF ablation in young patients with AF (<45 years of age) as in older patients.	IIa
Tachy-brady syndrome	It is reasonable to offer AF ablation as an alternative to pacemaker implantation in patients with tachy-brady syndrome.	IIa
Athletes with AF	It is reasonable to offer high-level athletes AF as first-line therapy due to the negative effects of medications on athletic performance.	IIa
Asymptomatic AF**	Paroxysmal: Catheter ablation may be considered in select patients.**	IIb
	Persistent: Catheter ablation may be considered in select patients.	IIb

Europace (2018) 20, 157–208

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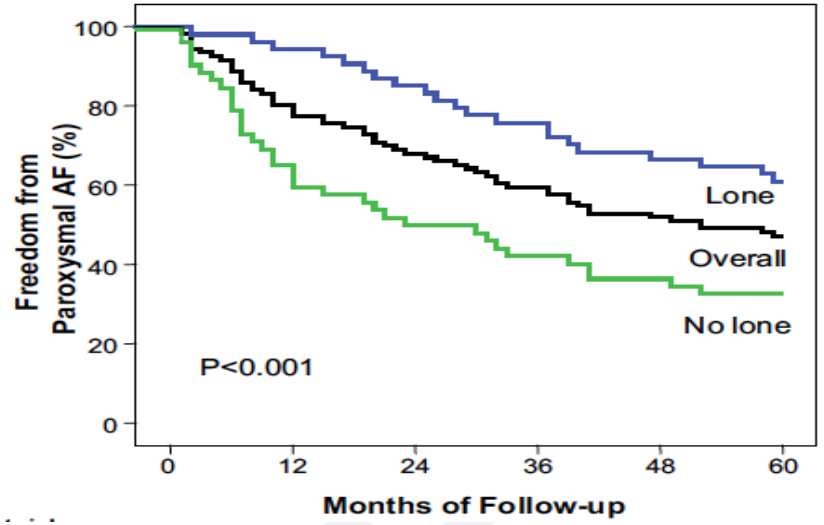
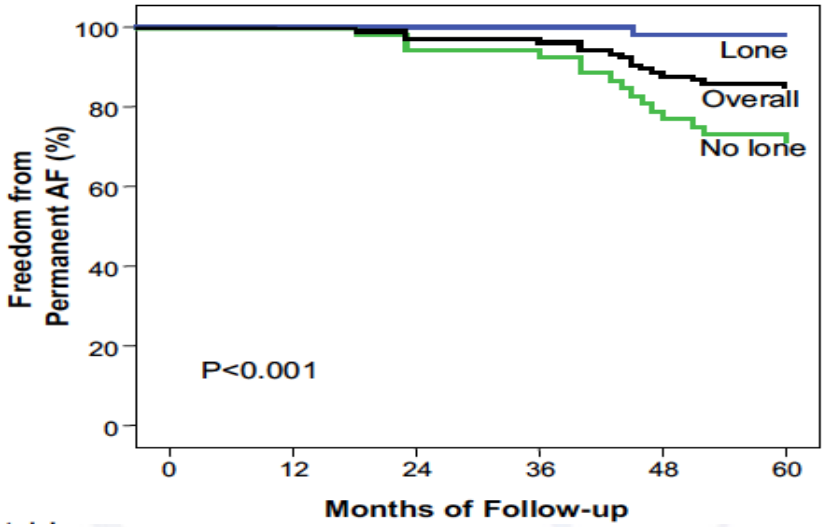
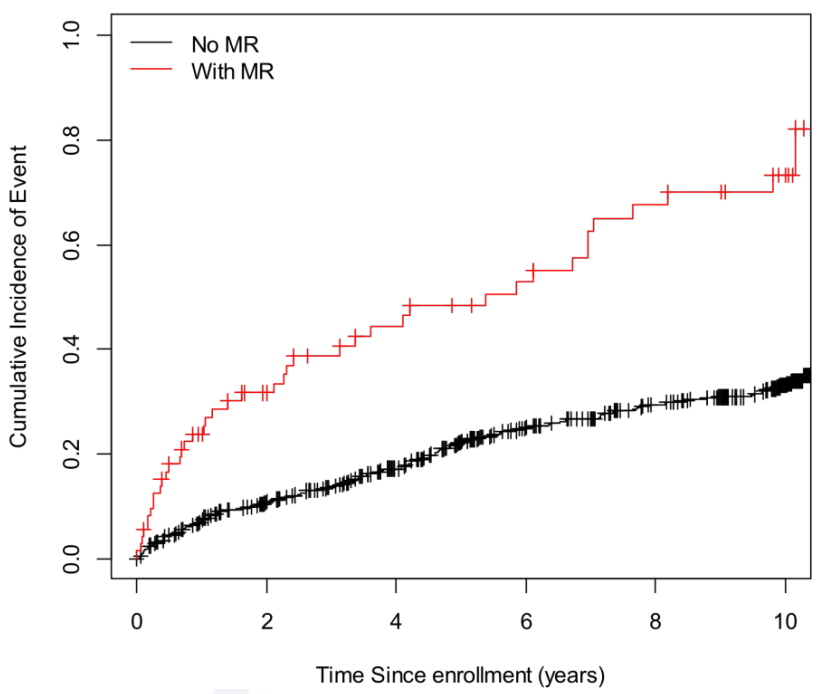
¿Cuál es la magnitud del problema? Historia natural de la FA.

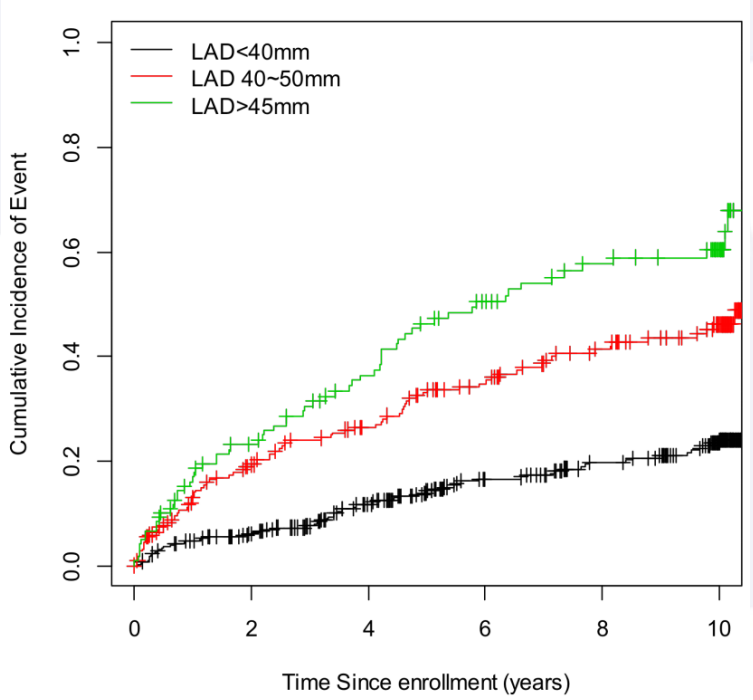




(Heart Rhythm 2008;5:1501–1507)

La FA es una patología que evoluciona.
Diferentes factores modulan su progresión en la clínica.





Heart Rhythm. 2017 Jun;14(6):801-807

¿Cuál es la magnitud del problema? Técnicas de ablación.

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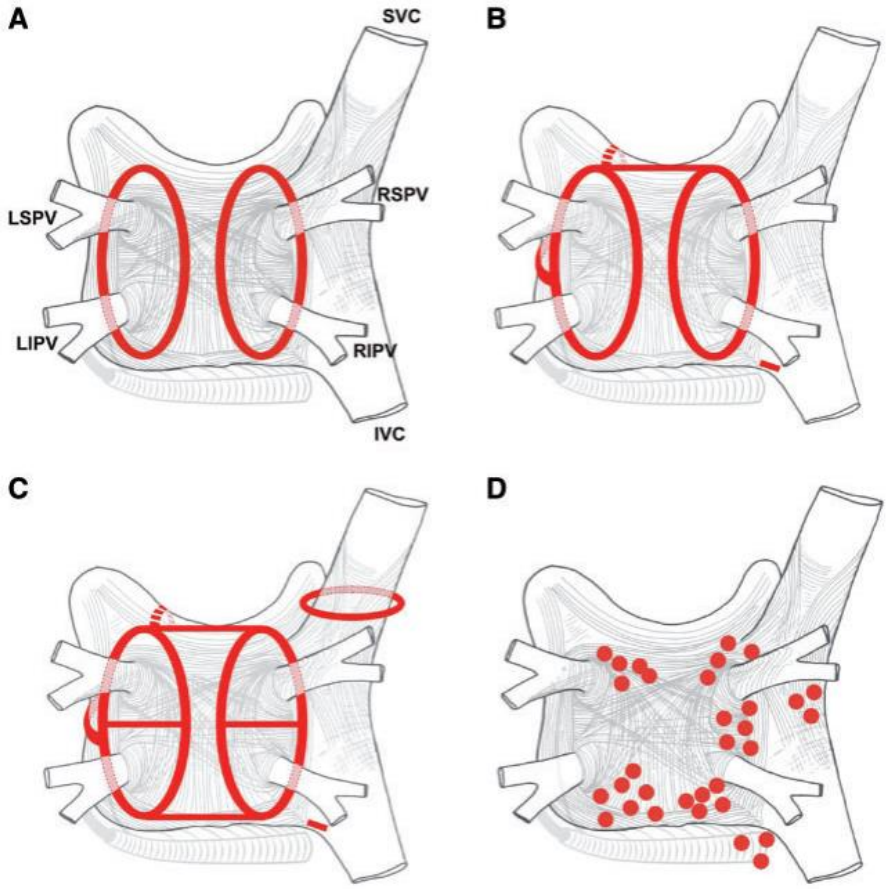
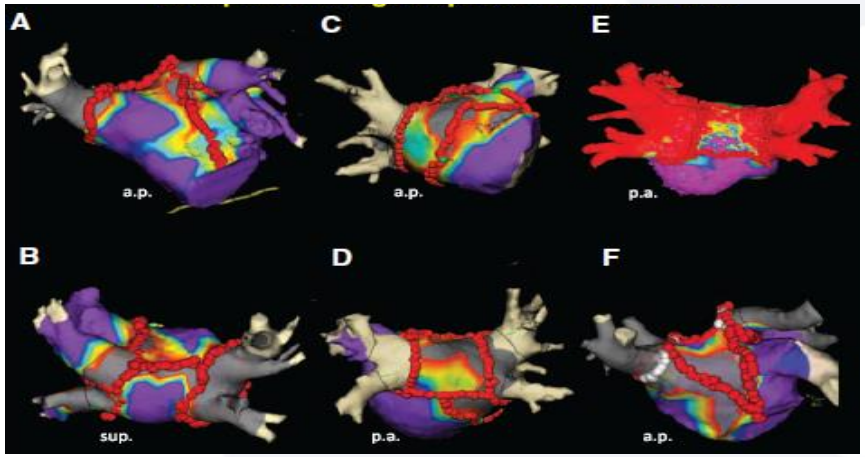
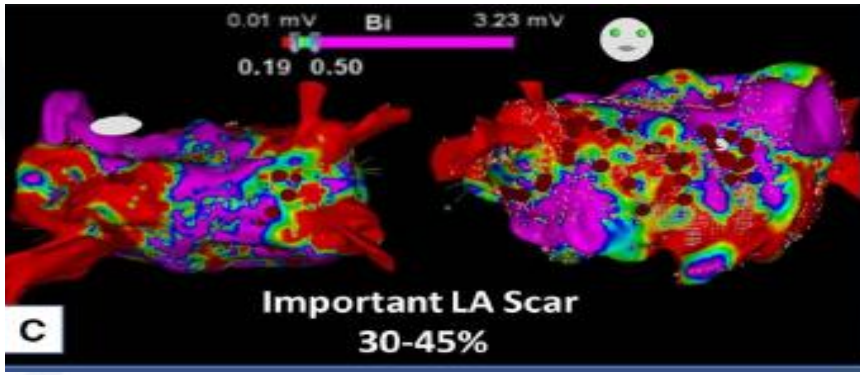
2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary



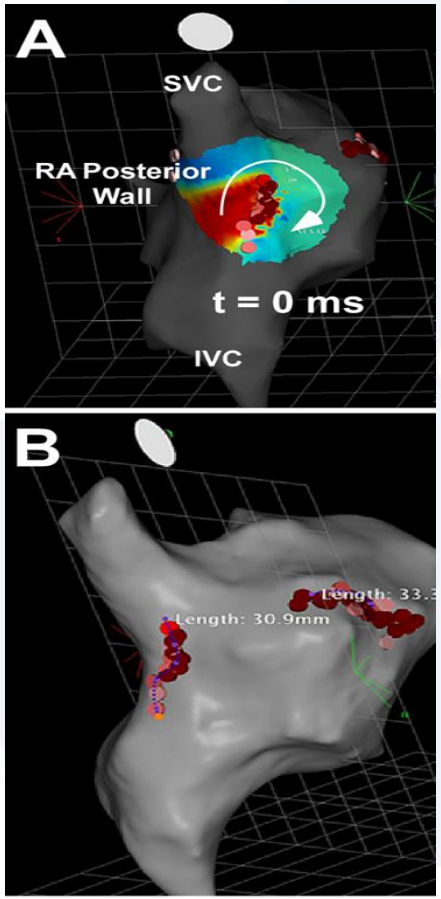
Europace (2018) 20, 157–208



(Circ Arrhythm Electrophysiol. 2014;7:825-833.)



Circ Arrhythm Electrophysiol. 2016;9:e002962.



Circ Arrhythm Electrophysiol. 2017 Dec;10(12). pii: e005740

- ***¿A quién?*** ***Son muchos!!!!!***

- ***¿Cuándo?*** ***La historia natural de la FA es evolutiva. ¿En que momento***

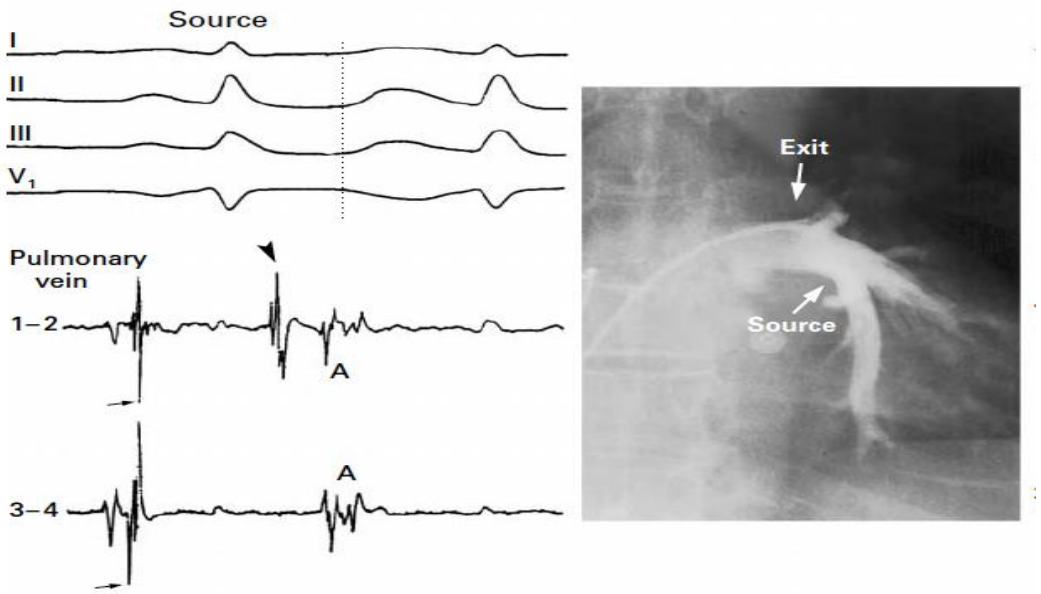
nos planteamos un procedimiento intervencionista? ¿Cómo afecta a los resultados?

- ***¿Cómo?*** ***La variedad de técnicas es amplia. ¿Cual debemos utilizar?***

¿Es sólo una cuestión de «catéter»? ¿Qué otros factores debemos tener en cuenta?

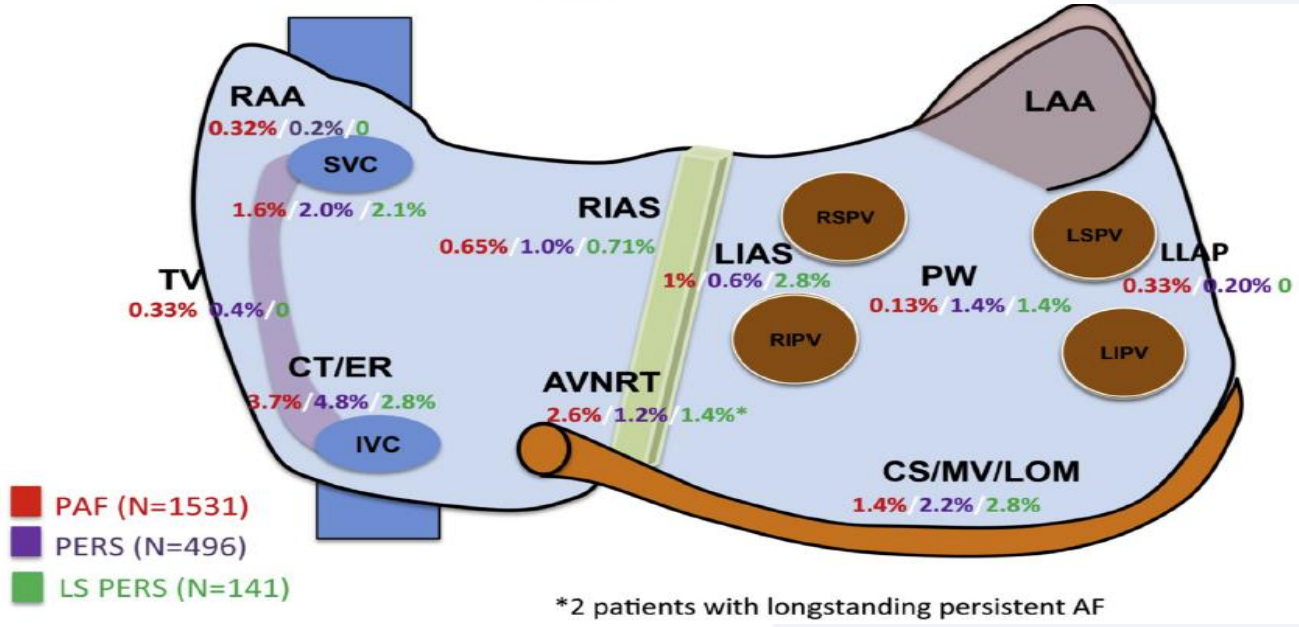
Atrial premature beats. The non-linear interaction with the substrate promote AF.

94% of atrial premature beats initiating AF become from the Pulmonary Veins



Haissaguerre et al. NEJM. 1998

Other foci are scattered through the atria

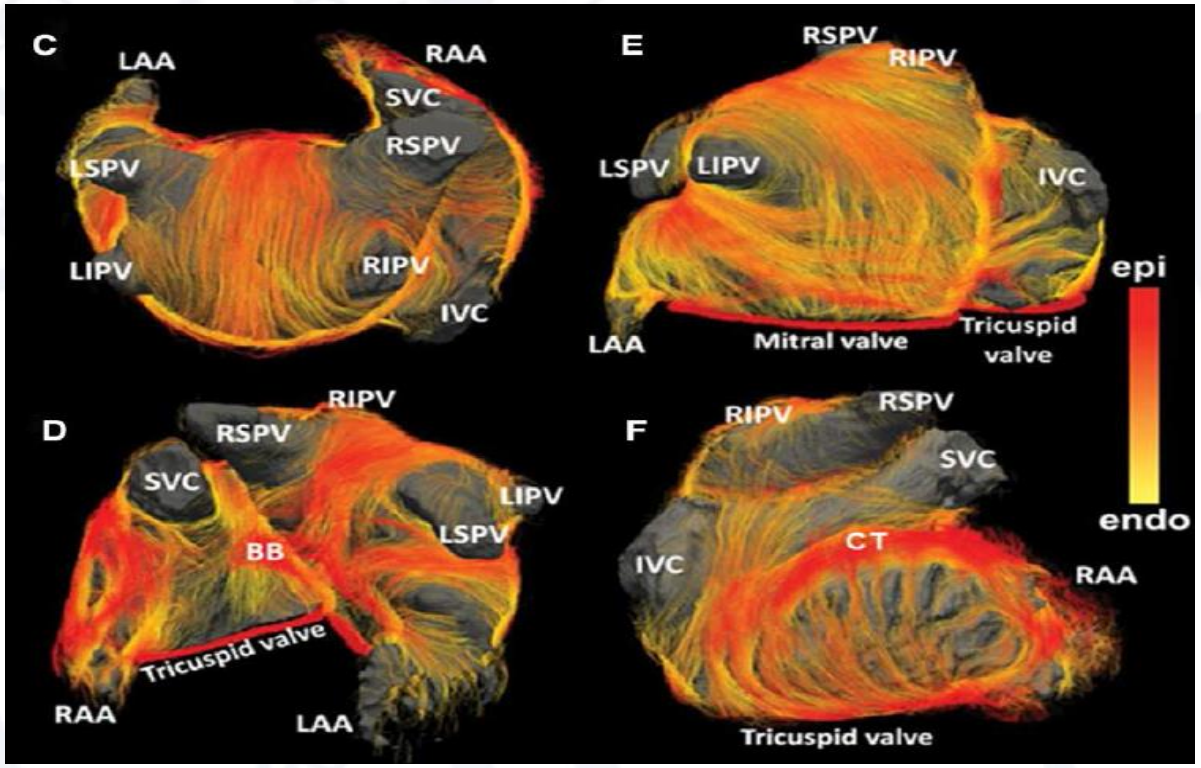


Santangeli P, et al. Heart Rhythm 2017

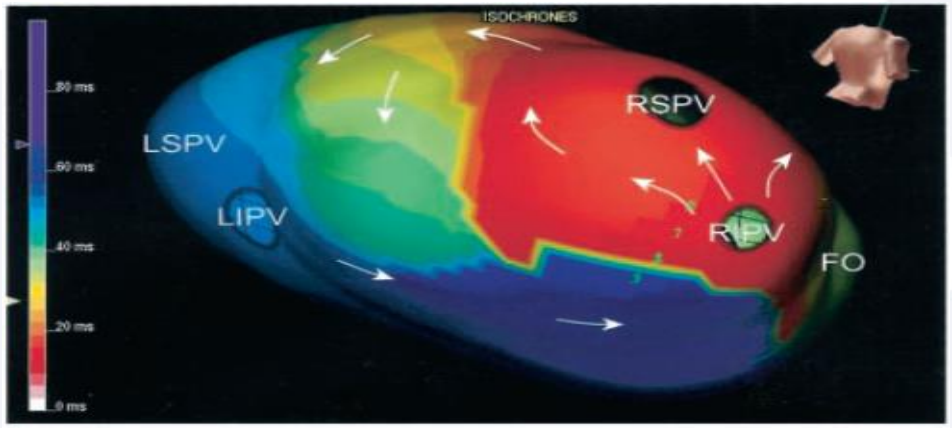
Several factors control de dynamic interaction of premature beats with the atrial tissue, from the ionic dimension (i.e., conditioning refractory periods) to the tissue level (i.e., fibrosis and fiber orientation).

Physiology of atrial depolarization. What does it mean for AF development?

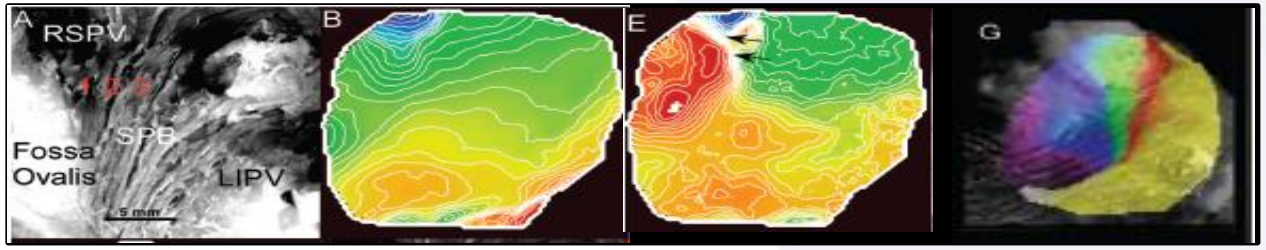
The P wave is the variation of potential field on the thoracic surface promoted by the *non-linear propagation* of depolarizing wave-fronts within the atria.



Pashakhanloo F, et al. Circ Arrhythm Electrophysiol. 2016.
Calvo D, Filgueiras D, Jalife J. Circ Arrhythm Electrophysiol. 2017.



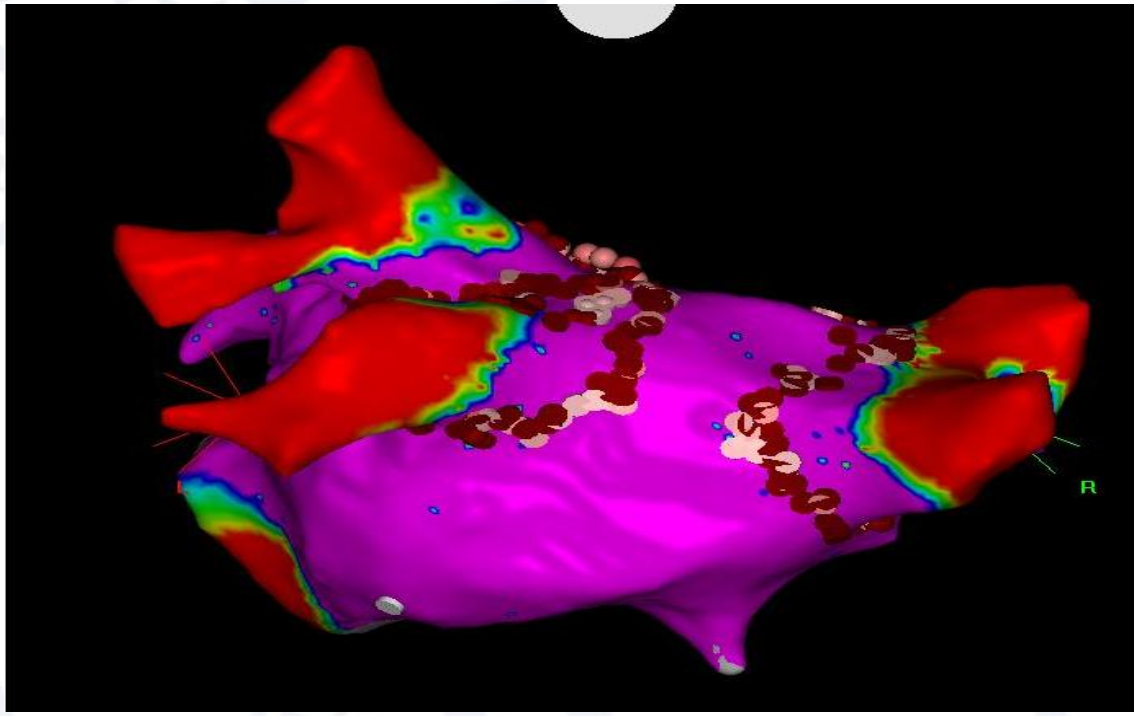
Markides V et al . Circulation. 2003.



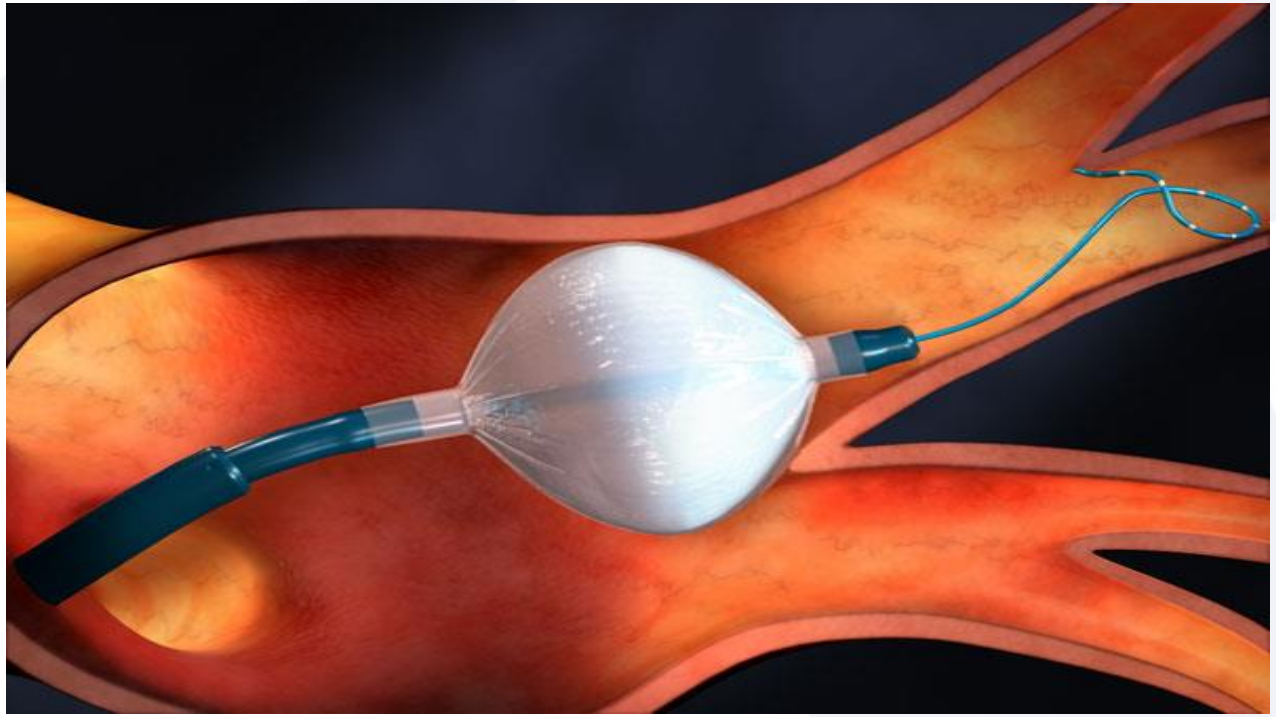
Kloss M, Calvo D, Jalife J. Circ Arrhythm Electrophysiol. 2008.

¡Just the normal atrial depolarization provides a substrate for functional reentry and AF development!

Radiofrecuencia



Crioablación



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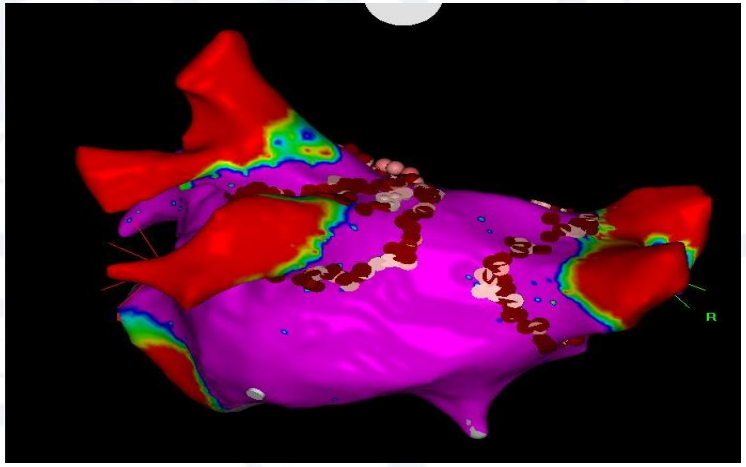
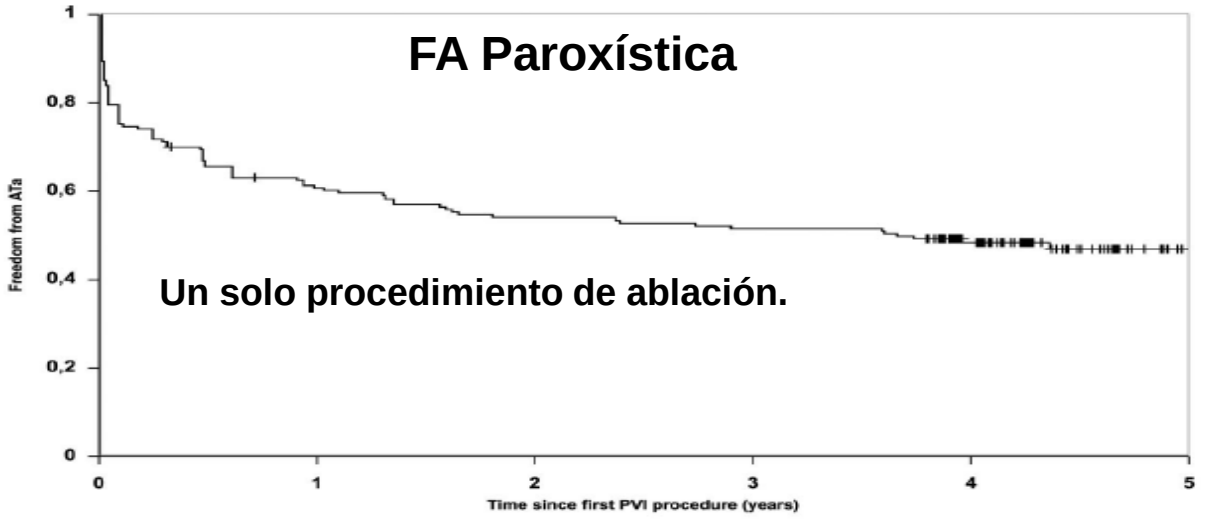
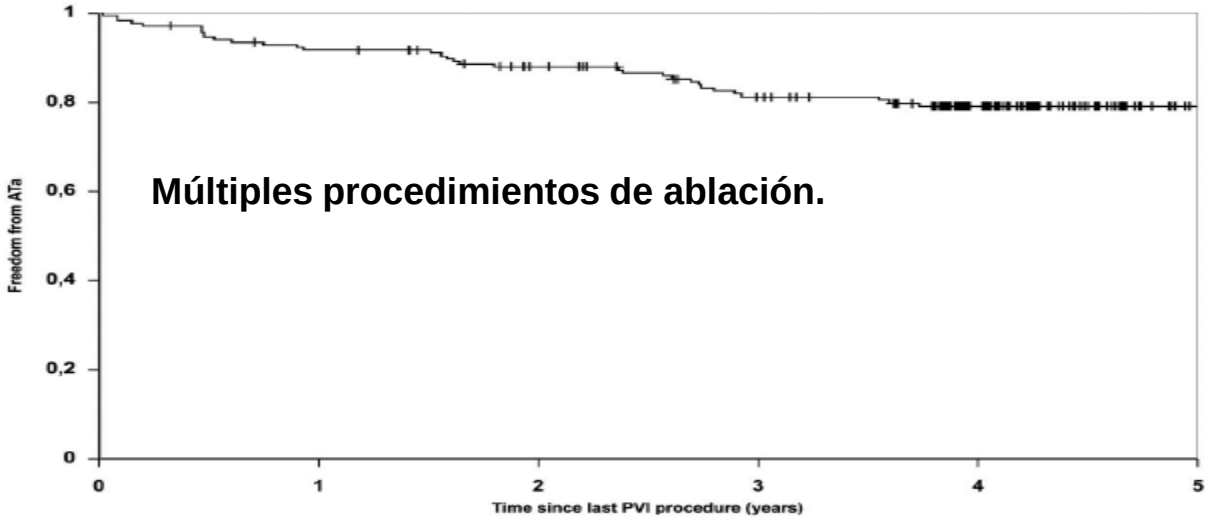
Resultados clínicos de la ablación de la FA.



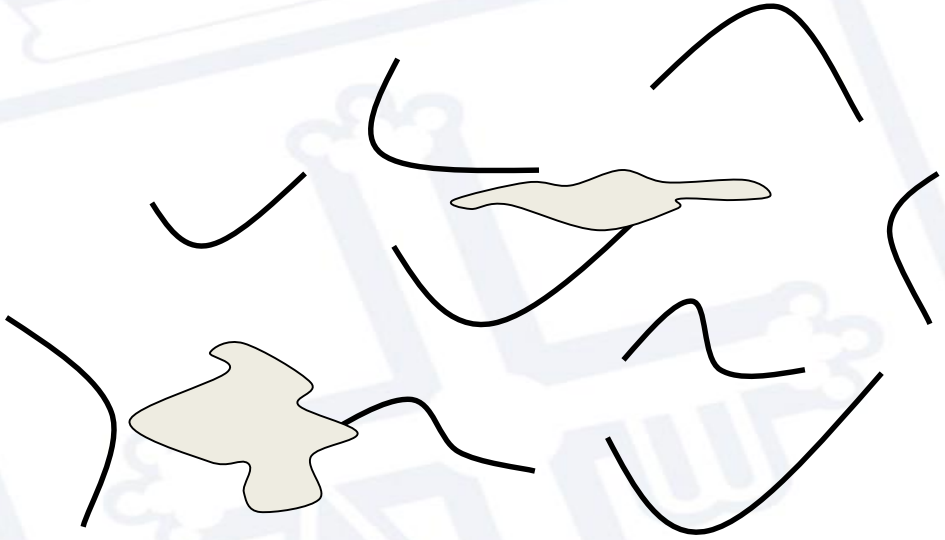




(*Circulation*. 2010;122:2368-2377.)

"Teoría de las múltiples ondas"

Moe et al postulated also that there were least requirements to allow fibrillation to be self-sustained. One such requirement was that ***a minimum number of propagating wavelets must be simultaneously exciting a tissue volume***, a hypothesis that seemed to fit well with the excellent results obtained subsequently by Cox et al using the surgical MAZE procedure (Cox et al., 1991).



Moe GK. 1956. Introductory remarks to part III of experimental methods for the evaluation of drugs in various disease states. Ann. NY Acad. Sci. 64:540–42

However, even if its assumptions were correct, the multiple wavelet hypothesis leaves **many unresolved questions**, including:

- What mechanisms explain the focal activity, wavebreak formation and reentry that usually occur during AF?
- How does the multiple wavelet hypothesis explain the hierarchical spatio-temporal organization that has been consistently demonstrated in animal models and humans over the last 20 years of research?
- More importantly, how does the multiple wavelet hypothesis explain the often-successful termination of AF by pulmonary vein isolation (PVI) and other highly localized ablation procedures in a significant number of patients? Finally, from a clinical point of view, ***the idea of randomness of wave propagation during AF introduces large uncertainties when trying to design effective therapy approaches, because whenever any target is addressed the outcome would be unpredictable***.

Calvo D & Filgueiras D & Jalife J. Pharm Reviews. 2018

Dos teorías mecanicistas tratan de explicar hoy la fibrilación cardiaca

Endo-Epicardial Dissociation

Maurit Allessie MD

- *The high-frequency activation during AF depends on a wide-spread endo-epicardial electrical dissociation that somehow promotes complex bidirectional conduction between the two layers of the atrial walls that behave functionally independently (de Groot et al., 2010).*
- *The emergent waves propagating from deeper layers break through each surface mimicking focal activity, while the dissociated propagation between endo and epicardium promotes self-sustainment of the activity (de Groot et al., 2010) (de Groot et al., 2016)*

Vs.

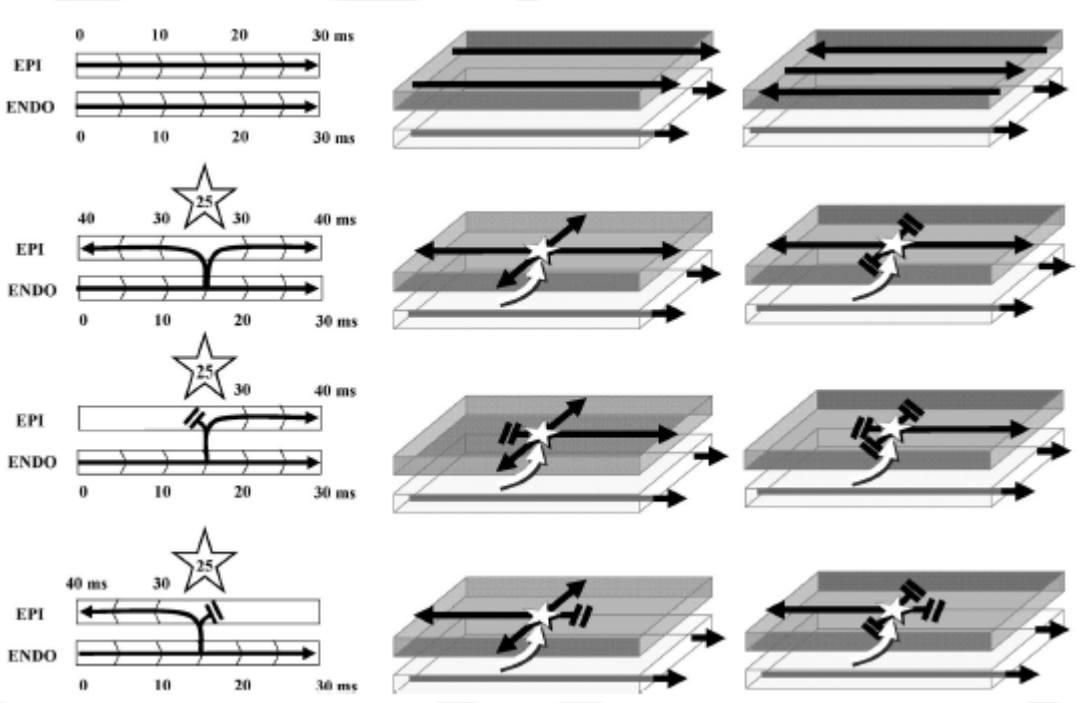
Spiral Reentrant Sources

- *Others support the theory of rotors, which gives predominance to a small number of localized functional reentrant sources (rotors) generating spiral waves (Jalife et al., 2002; Narayan et al., 2012).*
- *Such waves emerge at high frequency, propagating away from the rotor to interact with tissue heterogeneities and giving rise to complex patterns of non-uniform propagation termed "fibrillatory conduction" (Jalife et al., 2002).*

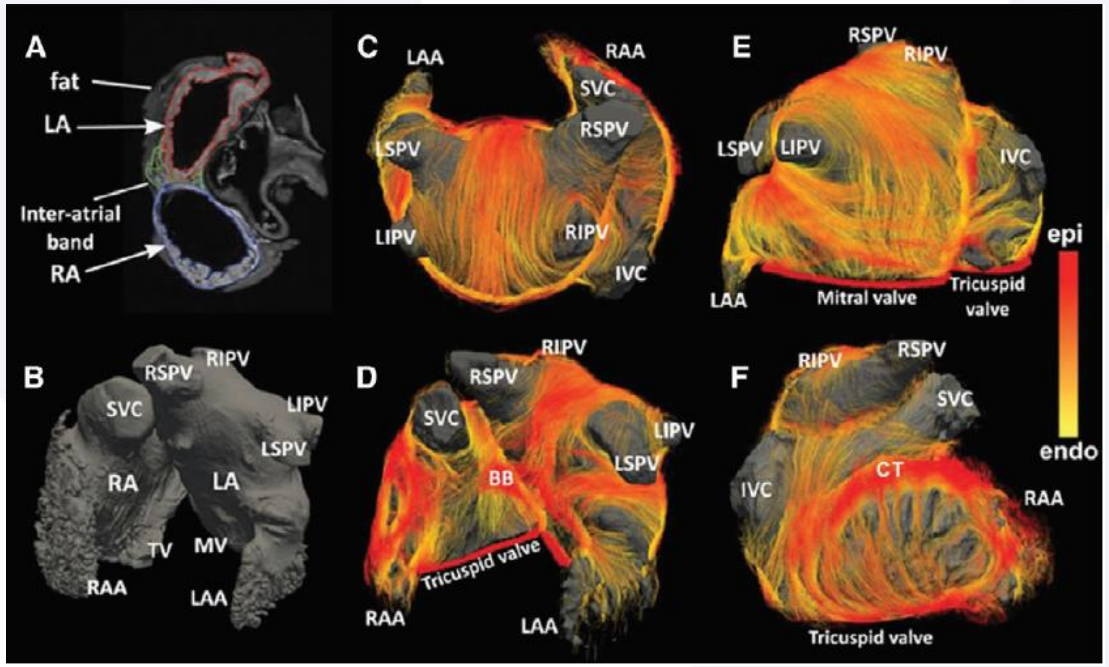
José Jalife, MD

Dos teorías mecanicistas tratan de explicar la fibrilación cardiaca

Endo-Epicardial Dissociation



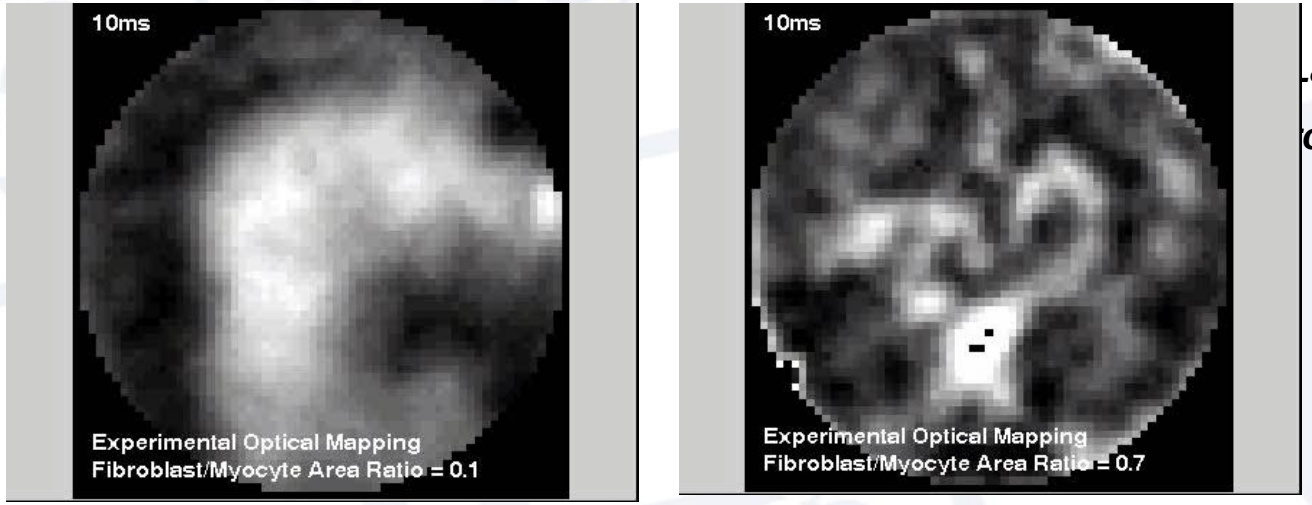
Allessie M & De Groot. Circulation AE. 2010



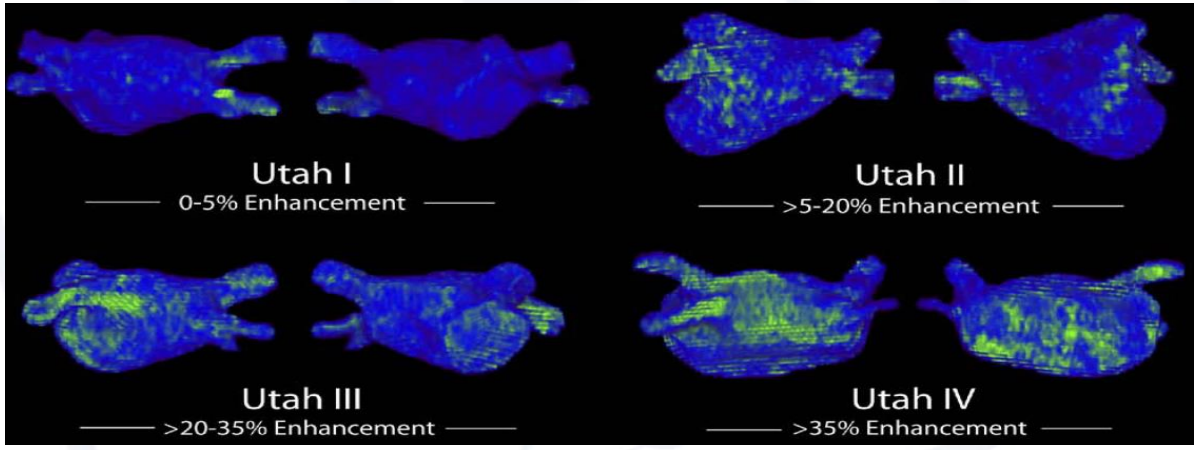
Pashakhanloo F, et al. Circ Arrhythm Electrophysiol. 2016.
Calvo D, Filgueiras D, Jalife J. Circ Arrhythm Electrophysiol. 2017.

Dos teorías mecanicistas tratan de explicar la fibrilación cardiaca

Spiral Reentrant Sources (Rotors)

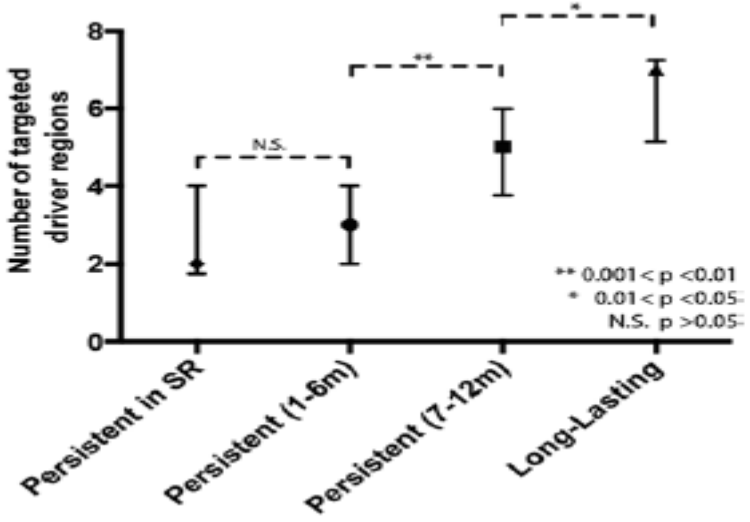


Zlochiver S. Biophys J, 2008.



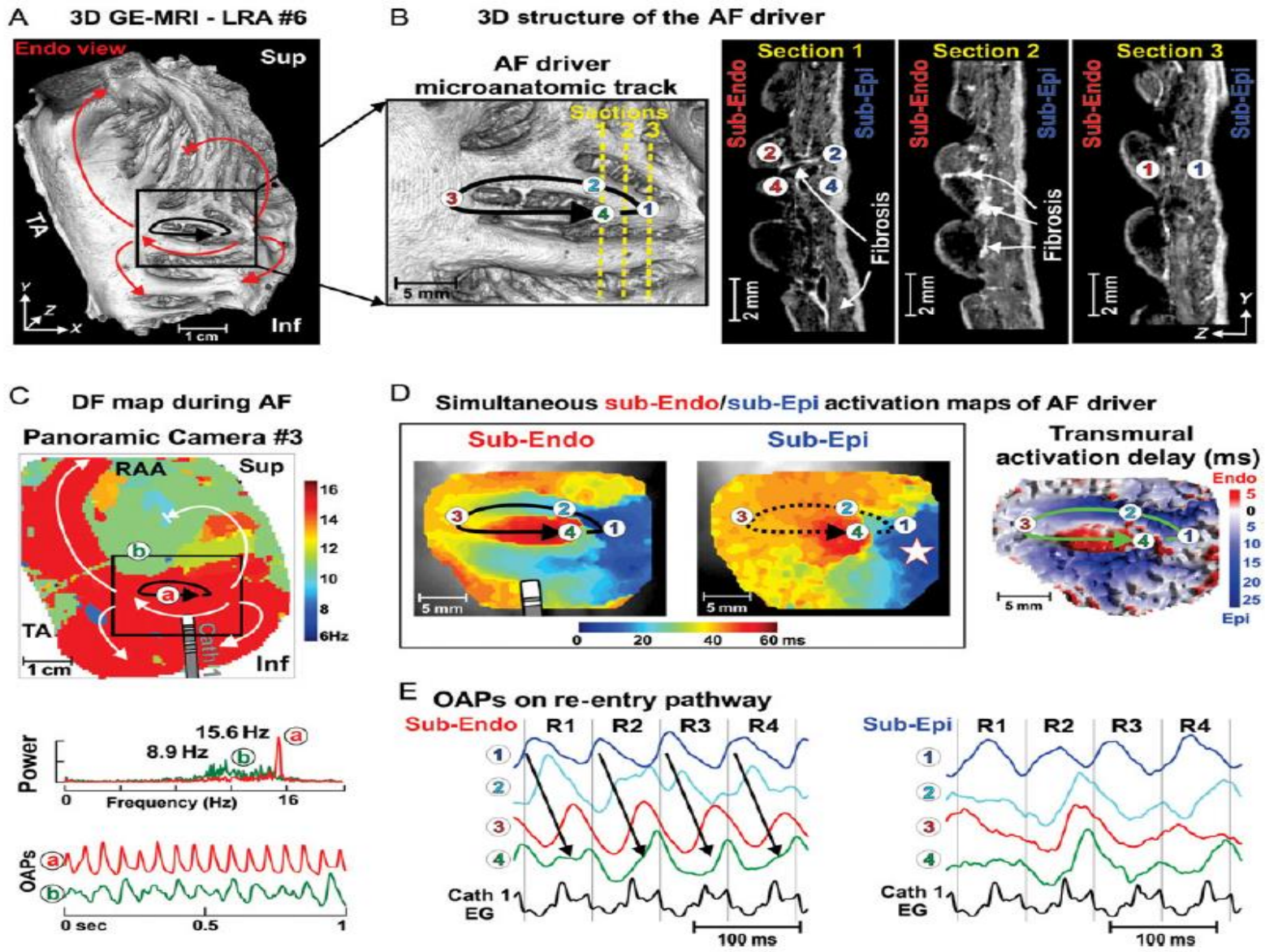
Mahnkopf & Marrouche. Heart Rhythm, 2010.

Las características del medio condicionan la dinámica de los rotores en la fibrilación cardiaca.



Haissaguerre M. CircAE, 2014.

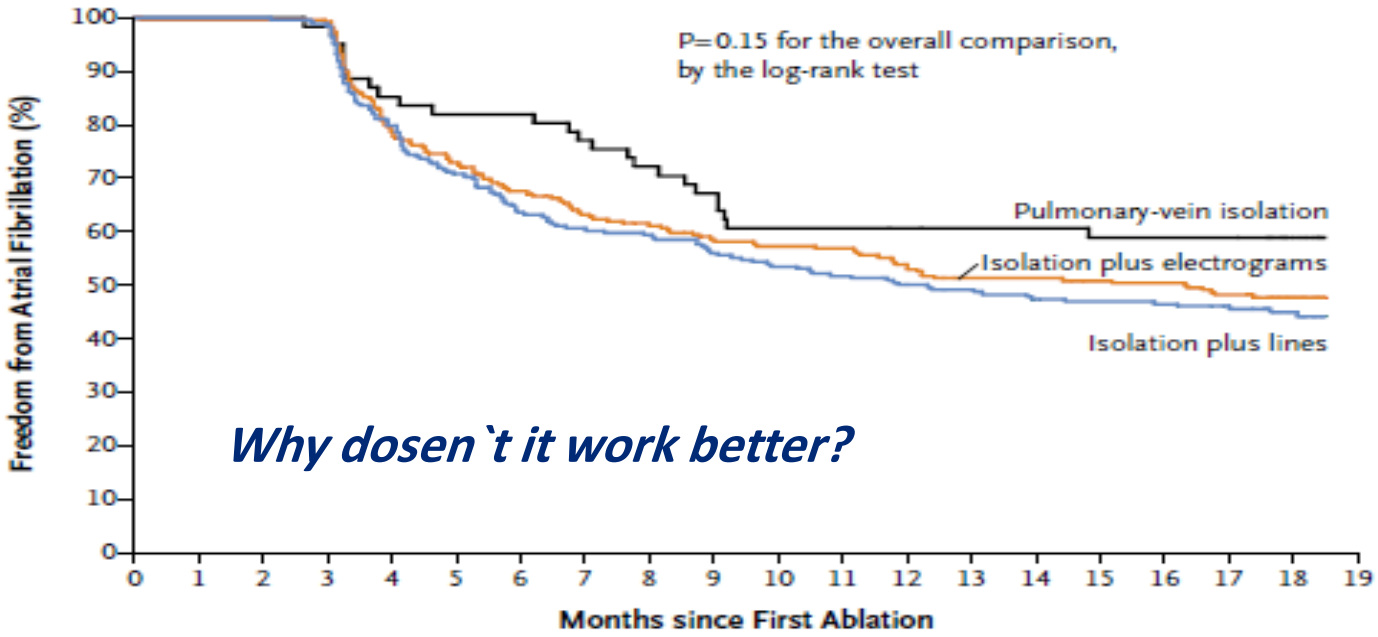
¿Oportunidades para la reconciliación?



Hansen BJ. EHJ, 2015.

Resultados clínicos de la ablación de la FA.

Approaches to Catheter Ablation for Persistent Atrial Fibrillation



Why dosen`t it work better?

No. at Risk						
Pulmonary-vein isolation	61	60	50	41	36	23
Isolation plus electrograms	244	242	161	137	124	72
Isolation plus lines	244	240	152	133	115	57

Figure 2. Freedom from Atrial Fibrillation.

N Engl J Med 2015;372:1812-22.

What can we do to improve results?

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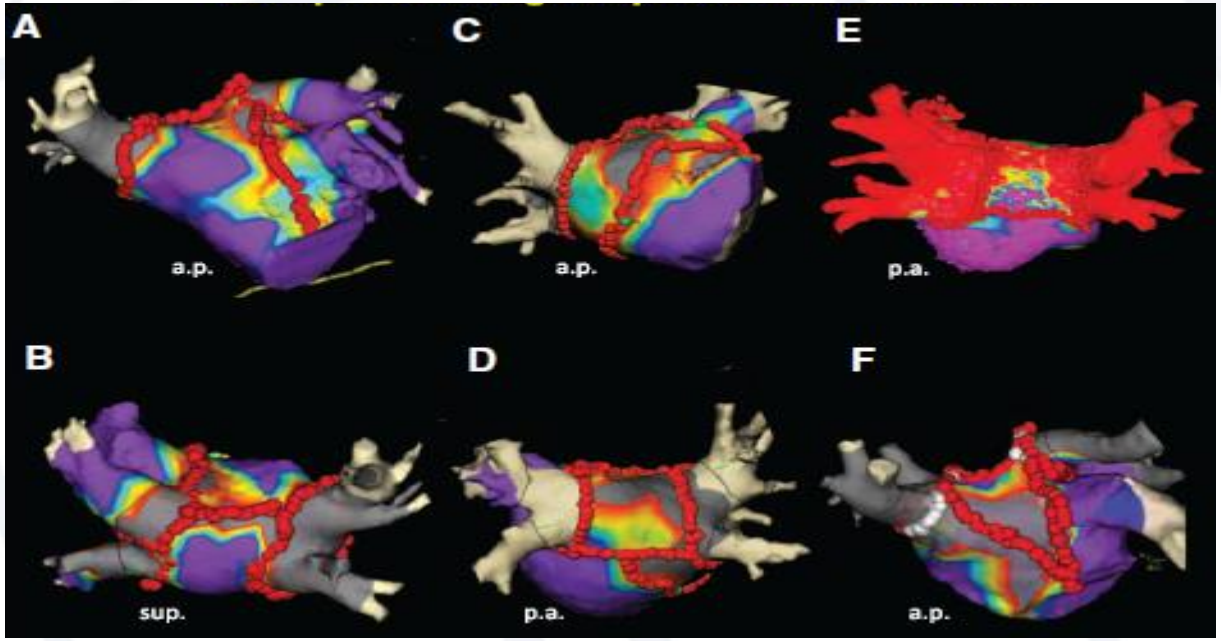
Tailored Atrial Substrate Modification Based on Low-Voltage Areas in Catheter Ablation of Atrial Fibrillation

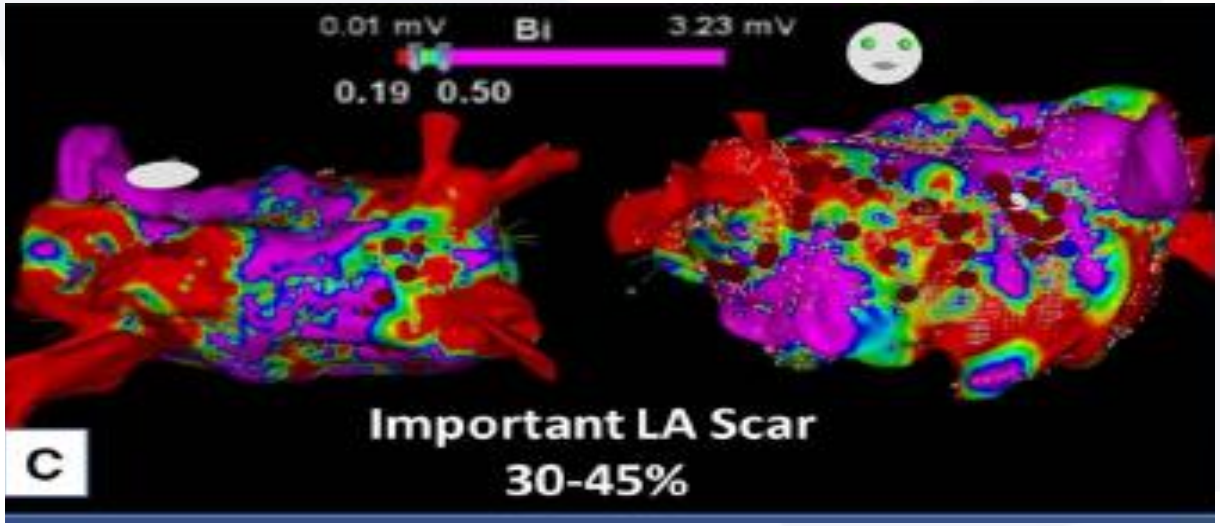
Sascha Rolf, MD; Simon Kircher, MD; Arash Arya, MD; Charlotte Eitel, MD; Philipp Sommer, MD; Sergio Richter, MD; Thomas Gaspar, MD; Andreas Bollmann, MD; David Altmann, MD; Carlos Piedra, MD; Gerhard Hindricks, MD; Christopher Piorkowski, MD



(*Circ Arrhythm Electrophysiol.* 2014;7:825-833.)

Ablation of Persistent Atrial Fibrillation Targeting Low-Voltage Areas With Selective Activation Characteristics

Amir S. Jadidi, MD; Heiko Lehrmann, MD; Cornelius Keyl, MD; Jérémie Sorrel, MD; Viktor Markstein, BSc; Jan Minners, MD; Chan-Il Park, MD; Arnaud Denis, MD; Pierre Jaïs, MD; Mélèze Hocini, MD; Clemens Potocnik, MD; Juergen Allgeier, MD; Willibald Hochholzer, MD; Claudia Herrera-Sidloky, MD; Steve Kim, MSEE; Youssef El Omri, MD; Franz-Josef Neumann, MD; Reinhold Weber, MD; Michel Haïssaguerre, MD; Thomas Arentz, MD



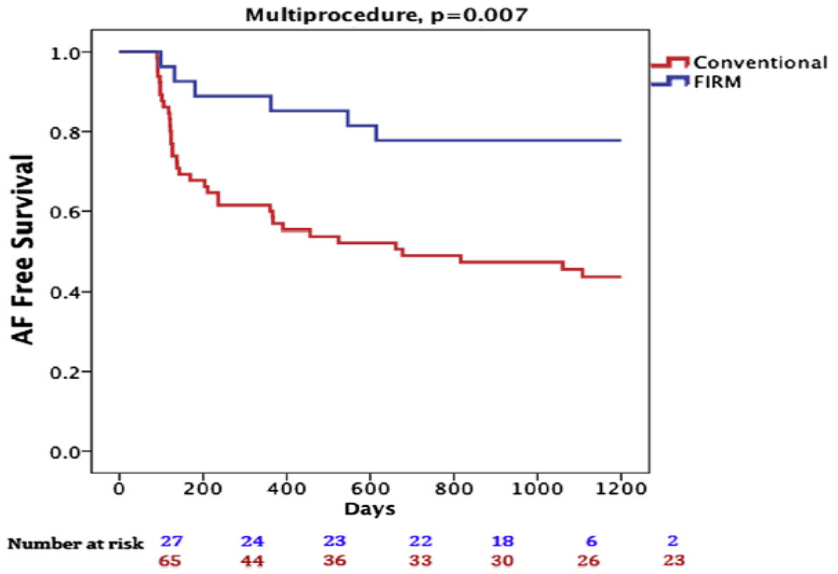
(*Circ Arrhythm Electrophysiol.* 2016;9:e002962.)

What can we do to improve results? The controversy of rotors.

Ablation of Rotor and Focal Sources Reduces Late Recurrence of Atrial Fibrillation Compared With Trigger Ablation Alone

Extended Follow-Up of the CONFIRM Trial (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation)

Sanjiv M. Narayan, MD, PhD,*† Tina Baykaner, MD,*† Paul Clopton, MS,† Amir Schricker, MD,*† Gautam G. Lalani, MD,*† David E. Krummen, MD,*† Kalyanam Shivkumar, MD, PhD,‡ John M. Miller, MD§

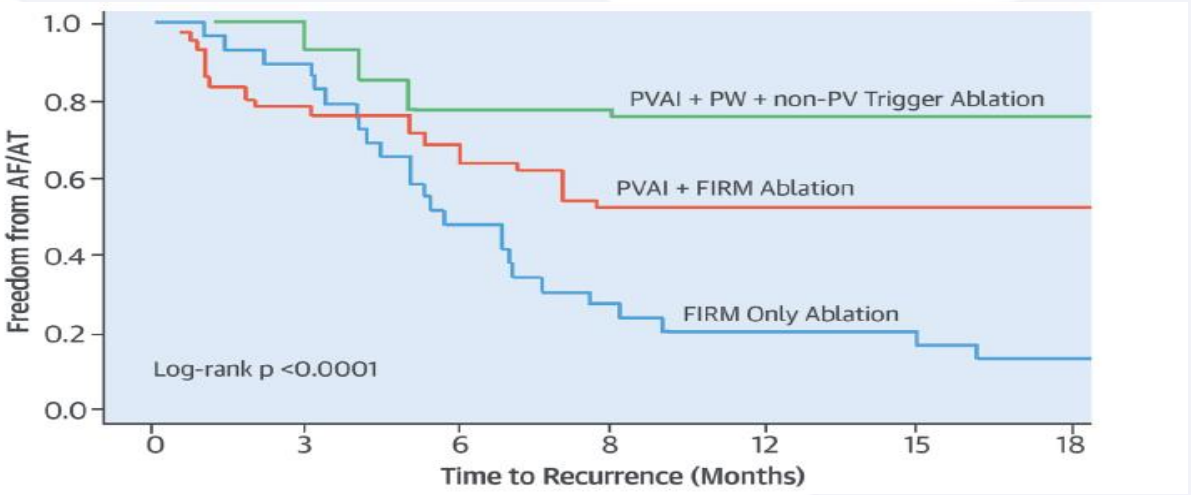


Narayan S. JACC, 2014.

Impact of Rotor Ablation in Nonparoxysmal Atrial Fibrillation Patients

Results From the Randomized OASIS Trial

Sanghamitra Mohanty, MD,[a] Carola Gianni, MD,[a] Prasant Mohanty, MBBS, MPH,[a] Philipp Halbfass, MD,[b] Tamara Metz, BSN, RN,[b] Chintan Trivedi, MD, MPH,[a] Thomas Deneke, MD,[b] Gery Tomassoni, MD,[c] Rong Bai, MD,[a,d] Amin Al-Ahmad, MD,[a] Shane Bailey, MD,[a] John David Burkhardt, MD,[a] G. Joseph Gallinghouse, MD,[a] Rodney Horton, MD,[a] Patrick M. Hranitzky, MD,[a] Javier E. Sanchez, MD,[a] Luigi Di Biase, MD, PhD,[a,b] Andrea Natale, MD[a,c,d,e,f,g,h,i]



Mohanty & Natale. JACC, 2016.
Retracted by JACC

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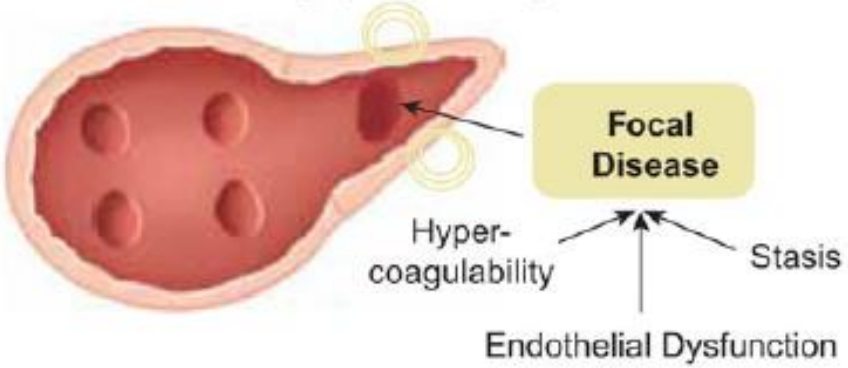
Podríamos contextualizar la FA en dos situaciones idealmente distintas

Focal Electrical Disease

Risk Factor

Reduced LA/LA Appendage Velocities

Atrial Dilatation/Myopathy ≈ Arrhythmia Burden



Temporal Association AF & Stroke
As needed Anticoagulation Plausible
Focal Therapy -> Lower Risk
Rhythm Treatments -> Lower Risk

Vs.

Systemic Disease Symptom

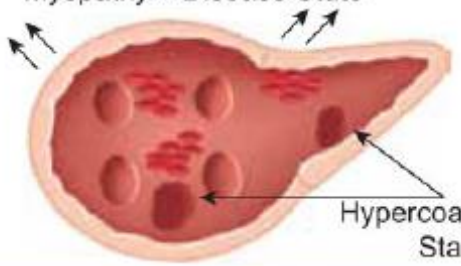
Risk Marker

Obesity — Vascular Disease — Sedentary Lifestyle

Metabolic Syndrome
Sleep Apnea
Diabetes
Hypertension

Arterial Stiffness
Microvascular Dysfunction
Diastolic Dysfunction

Atrial Dilatation/Fibrosis/ Myopathy ≈ Disease State

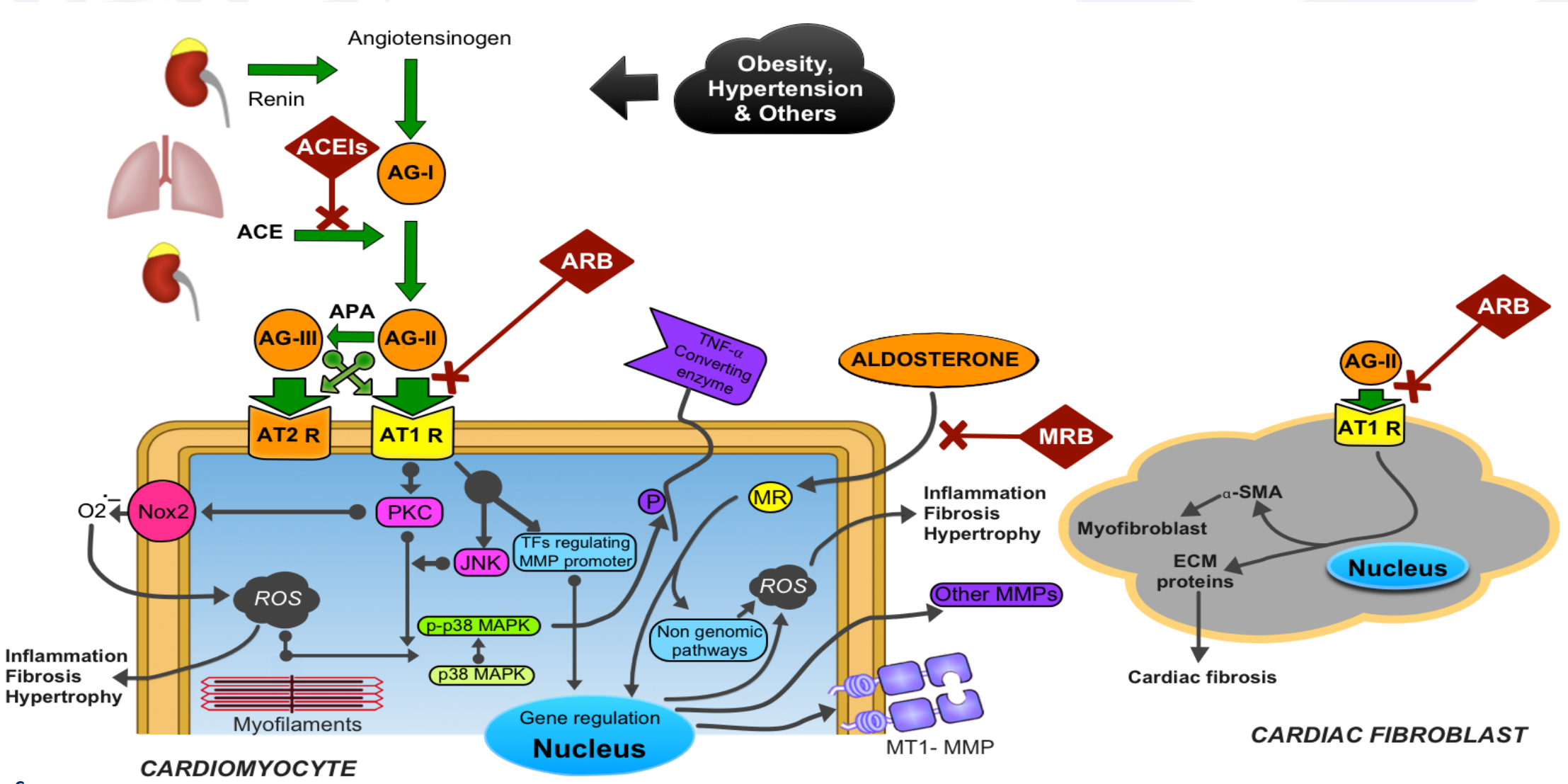


Poor Temporal Association AF & Stroke
Systemic Therapy-> Lower Risk
Risk Persists Despite Rhythm Treatment

David Calvo Cuervo
Unidad de Arritmias. Área del Corazón. HUCA

Bunch TJ. European Heart Journal 2016

Fisiología de la FA.



David Calvo Cuervo
Unidad de Arritmias. Área del Corazón. HUCA

Calvo D & Filgueiras D & Jalife J. Pharm Reviews. 2018

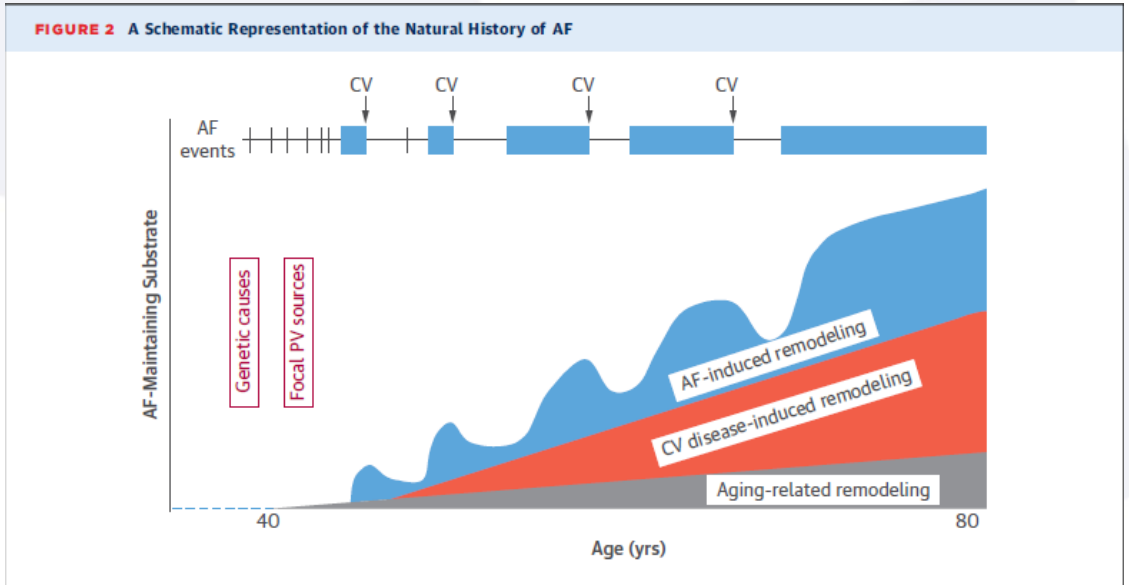
Fisiología de la FA.

HOSPITAL UNIVERSITARIO CENTRAL de ASTURIAS

Es difícil pensar que el pronóstico de la FA sea el mismo ante sustratos patológicos muy distintos.

	EHRAS class			
	I	II	III	IV
Type of Atrial Cardiomyopathy	Cardiomyocyte	Fibrosis	Fibrosis + cardiomyocyte	Non collagen infiltrate
Lone AF		✔	✔	
Atrial amyloidosis				✔
Muscular dystrophies	✔	✔	✔	✔
Congestive heart failure		✔	✔	✔
Obstructive sleep apnea	✔		✔	
AF-induced remodeling	✔		✔	
Drug-induced	✔	✔	✔	✔
Myocarditis			✔	✔
Age		✔		
High blood pressure	✔	✔	✔	
Obesity			✔	✔
Diabetes mellitus	✔		✔	✔
Valvular heart disease	✔	✔	✔	✔

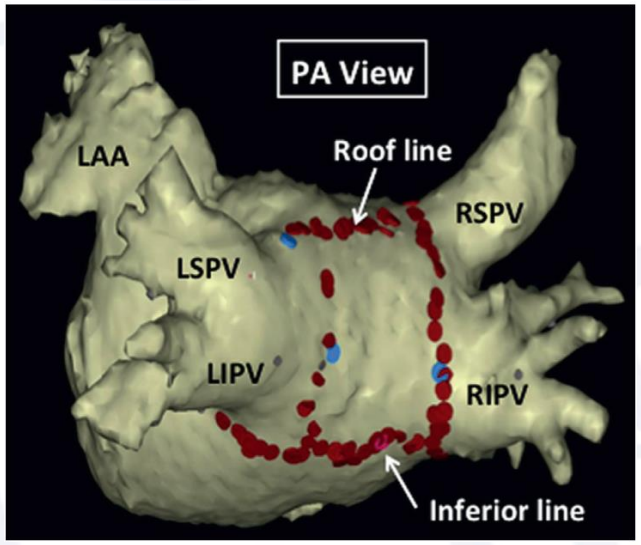
Goette A, Kalman JM, Aguinaga L, et al. EHRA/ HRS/APHRS/SOLAECE expert consensus on atrial cardiomyopathies: definition, characterization, and clinical implication. Heart Rhythm 2017;14:e3–40

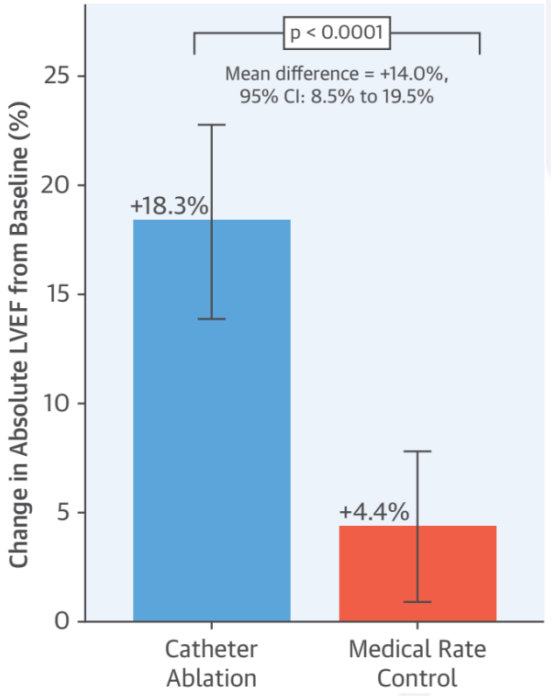


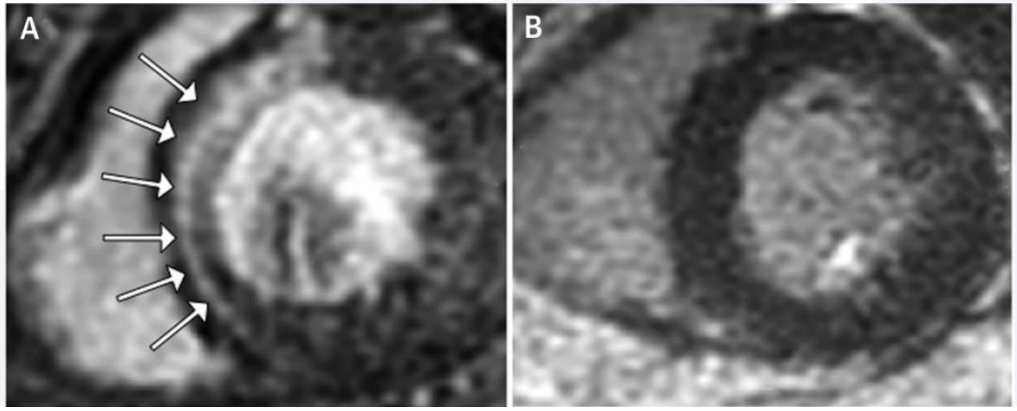
Nattel S. JACC. 2017

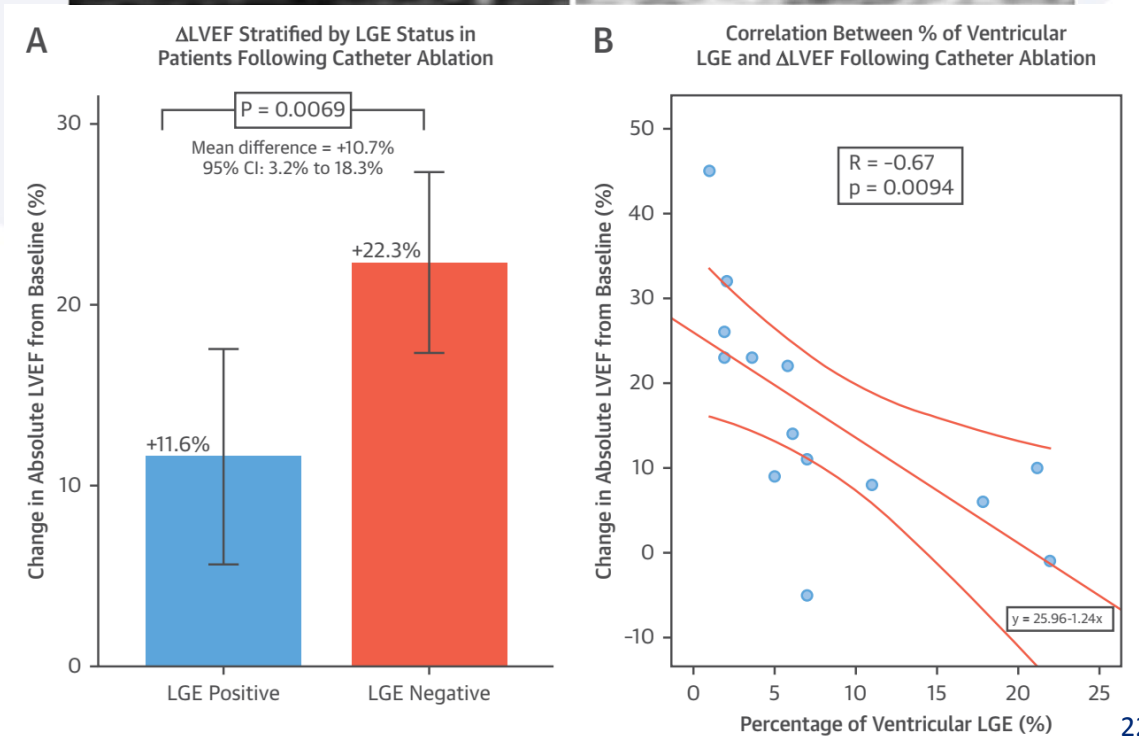
Catheter Ablation Versus Medical Rate Control in Atrial Fibrillation and Systolic Dysfunction

The CAMERA-MRI Study







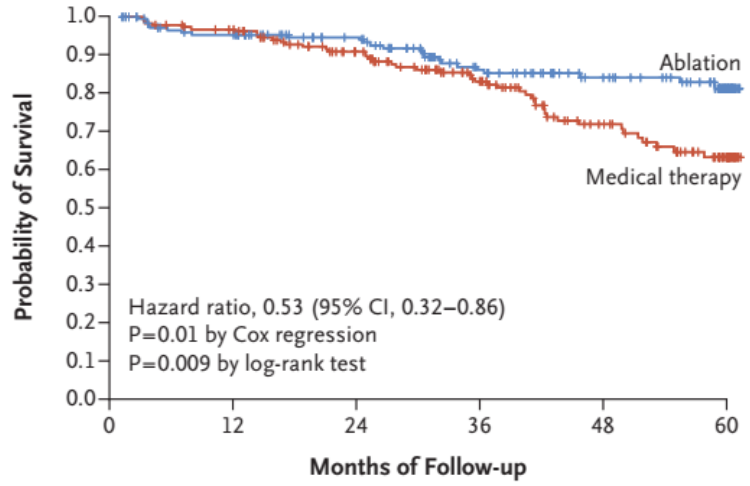


J Am Coll Cardiol. 2017 Oct 17;70(16):1949-1961
JACC Clin Electrophysiol. 2018 Aug;4(8):999-1007

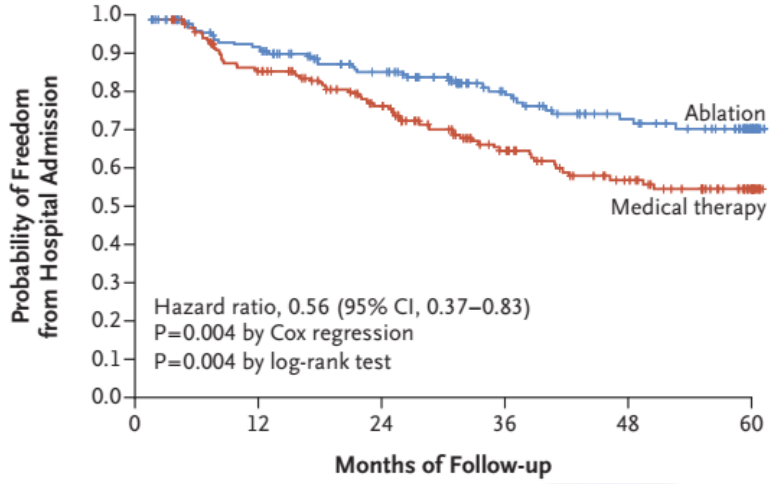
HOSPITAL UNIVERSITARIO CENTRAL de ASTURIAS

CASTLE-AF trial: Catheter Ablation for AF with Heart Failure

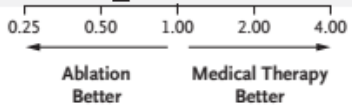
B Death from Any Cause



C Hospitalization for Worsening Heart Failure



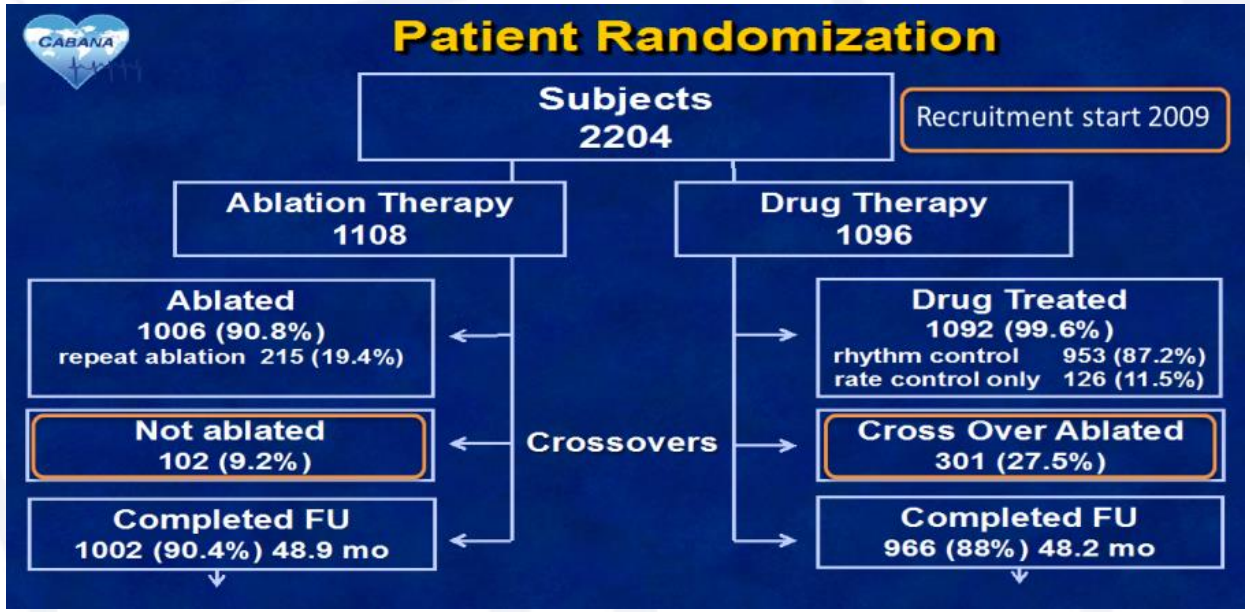
Subgroup	Ablation	Medical Therapy	Hazard Ratio (95% CI)	Interaction
	no. of events/no. of patients			
Type of atrial fibrillation				0.90
Paroxysmal	17/54	34/64	0.60 (0.34–1.08)	
Persistent	34/125	48/120	0.64 (0.41–0.99)	
CRT–D implanted				0.60
No	37/131	57/132	0.65 (0.43–0.98)	
Yes	14/48	25/52	0.54 (0.28–1.04)	
ICD indication				0.20
Primary	43/160	72/163	0.57 (0.39–0.83)	
Secondary	8/19	10/21	1.03 (0.41–2.62)	
Sex				0.36
Female	9/23	12/29	0.93 (0.39–2.21)	
Male	42/156	70/155	0.58 (0.39–0.84)	
Age				0.17
<65 yr	18/96	34/99	0.48 (0.27–0.85)	
≥65 yr	33/83	48/85	0.79 (0.50–1.23)	
NYHA functional class				0.06
II	20/101	46/109	0.42 (0.25–0.72)	
III	22/50	26/49	0.89 (0.51–1.58)	
LVEF				0.01
<25%	20/34	15/27	1.36 (0.69–2.65)	
≥25%	29/130	61/145	0.48 (0.31–0.74)	
Cause of heart failure				0.56
Nonischemic	26/107	29/88	0.74 (0.43–1.25)	
Ischemic	25/72	53/96	0.60 (0.37–0.97)	
Diabetes				0.06
No	32/136	48/117	0.52 (0.33–0.81)	
Yes	19/43	34/67	1.01 (0.58–1.78)	
Hypertension				0.88
No	12/50	19/48	0.59 (0.28–1.21)	
Yes	39/129	63/136	0.63 (0.42–0.93)	
Amiodarone use				0.66
No	37/122	61/133	0.65 (0.43–0.97)	
Yes	13/55	18/46	0.55 (0.27–1.13)	
Digitalis use				0.68
No	41/146	52/124	0.65 (0.43–0.98)	
Yes	9/31	27/56	0.56 (0.26–1.19)	
Beta-blocker use				0.47
No	4/12	4/9	1.01 (0.25–4.05)	
Yes	46/165	75/171	0.60 (0.42–0.87)	

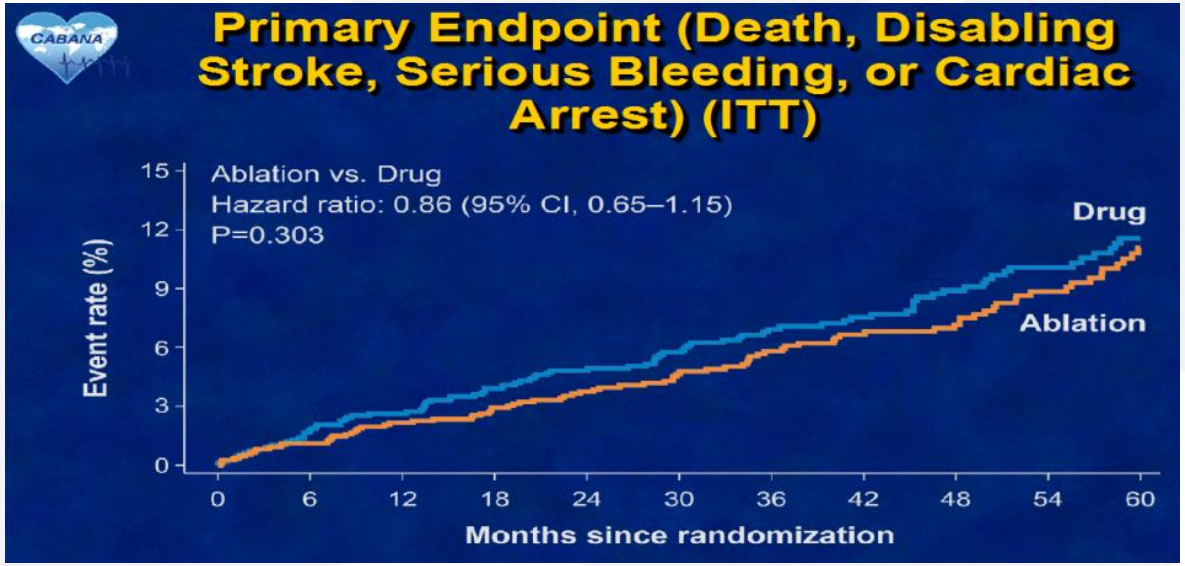


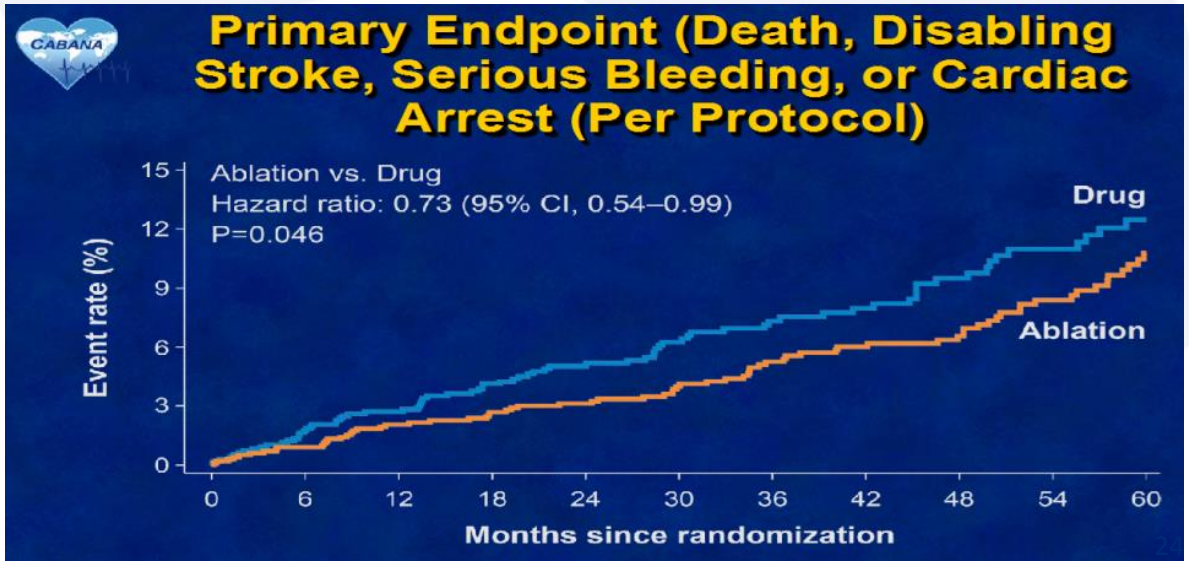
HOSPITAL UNIVERSITARIO CENTRAL de ASTURIAS

Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) Trial: Study Rationale and Design

Am Heart J. 2018 May;199:192-199

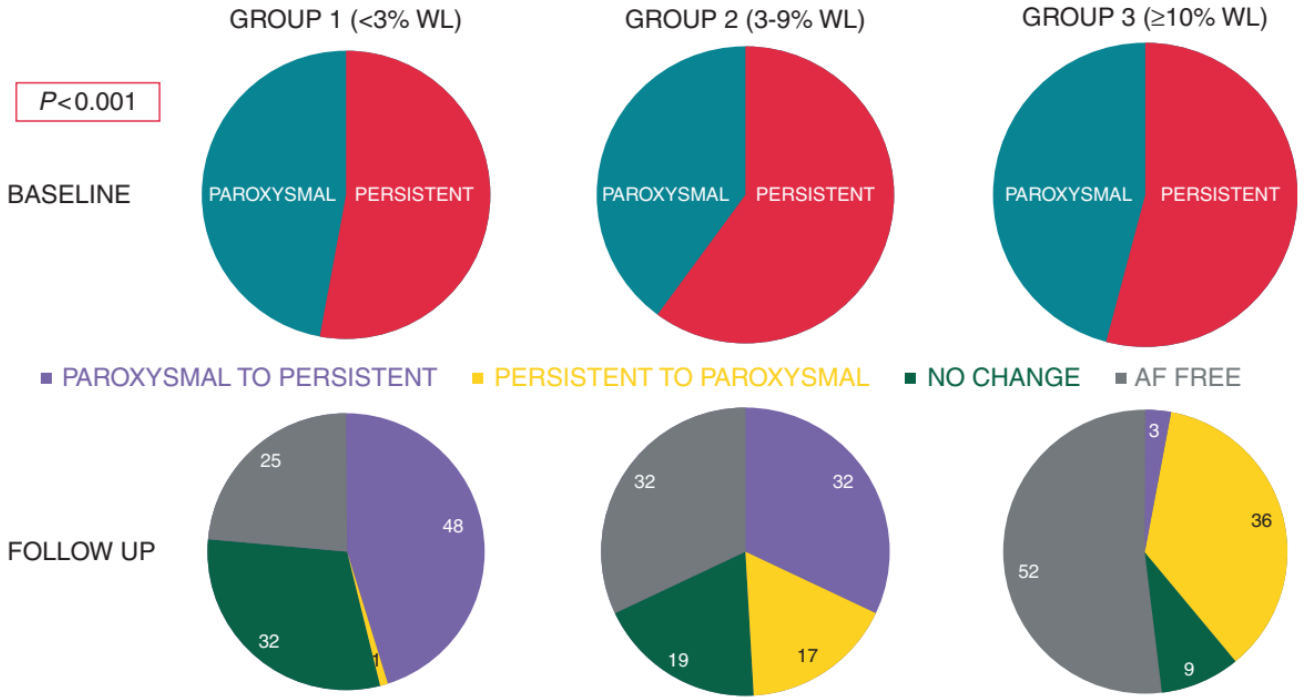






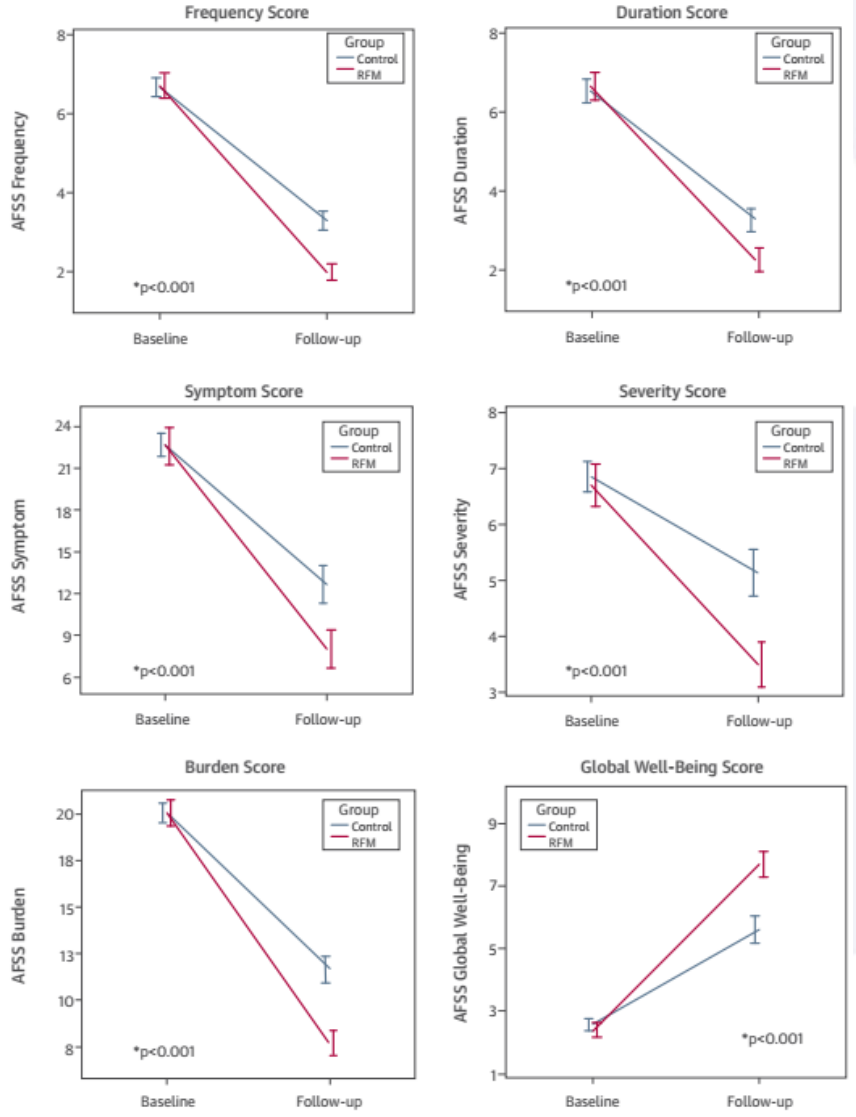
HOSPITAL UNIVERSITARIO CENTRAL de ASTURIAS

PREVEntion and regReSsive Effect of weight-loss and risk factor modification on Atrial Fibrillation: the REVERSE-AF study



Europace. 2018 Jun 14. doi: 10.1093/europace/euy117

The ARREST-AF Cohort Study

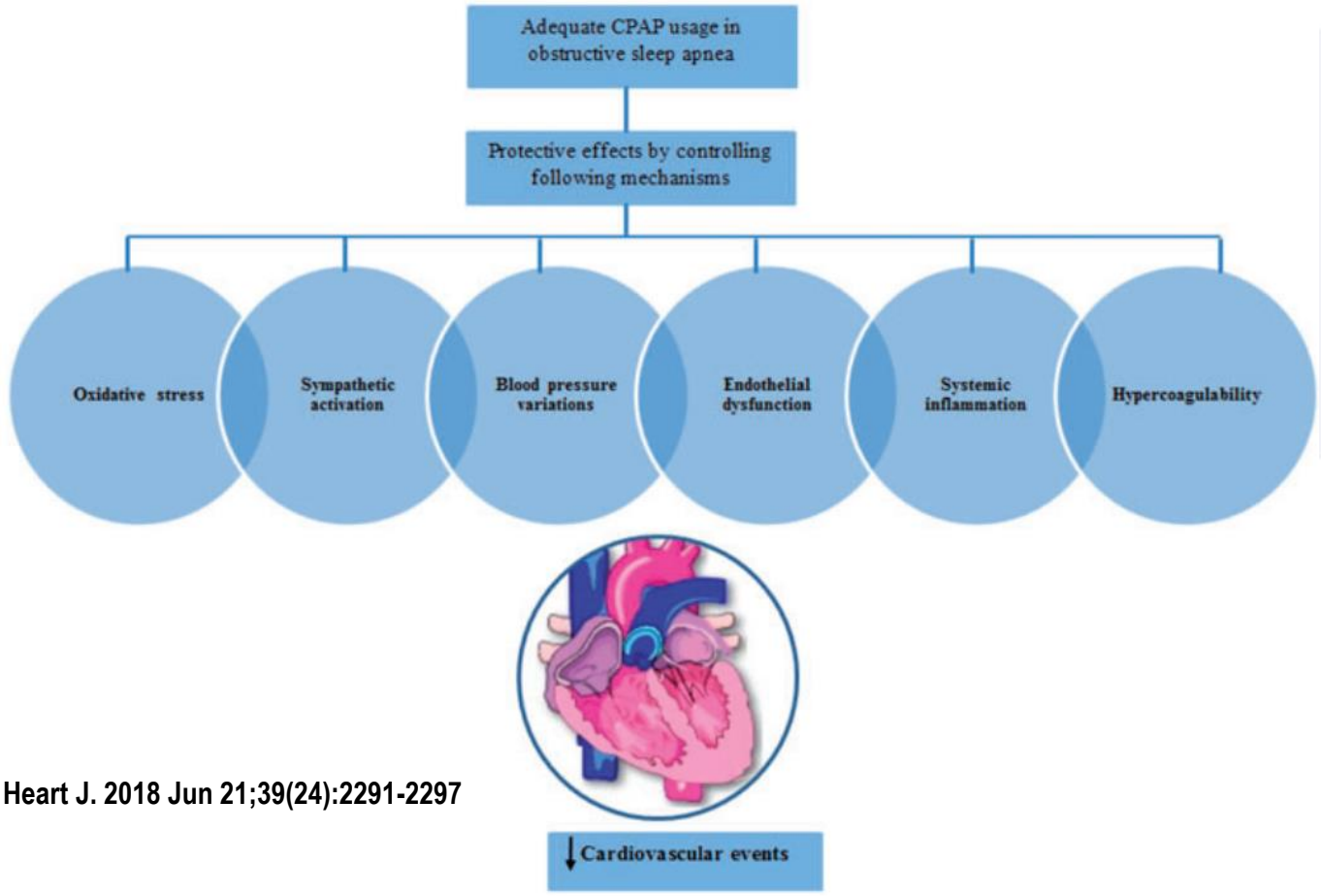


J Am Coll Cardiol. 2014 Dec 2;64(21):2222-31

Ablación de la FA. Algo más que catéter.

HOSPITAL UNIVERSITARIO CENTRAL de ASTURIAS

A meta-analysis of continuous positive airway pressure therapy in prevention of cardiovascular events in patients with obstructive sleep apnoea



Eur Heart J. 2018 Jun 21;39(24):2291-2297

Treatment of Obstructive Sleep Apnea Reduces the Risk of Atrial Fibrillation Recurrence After Catheter Ablation

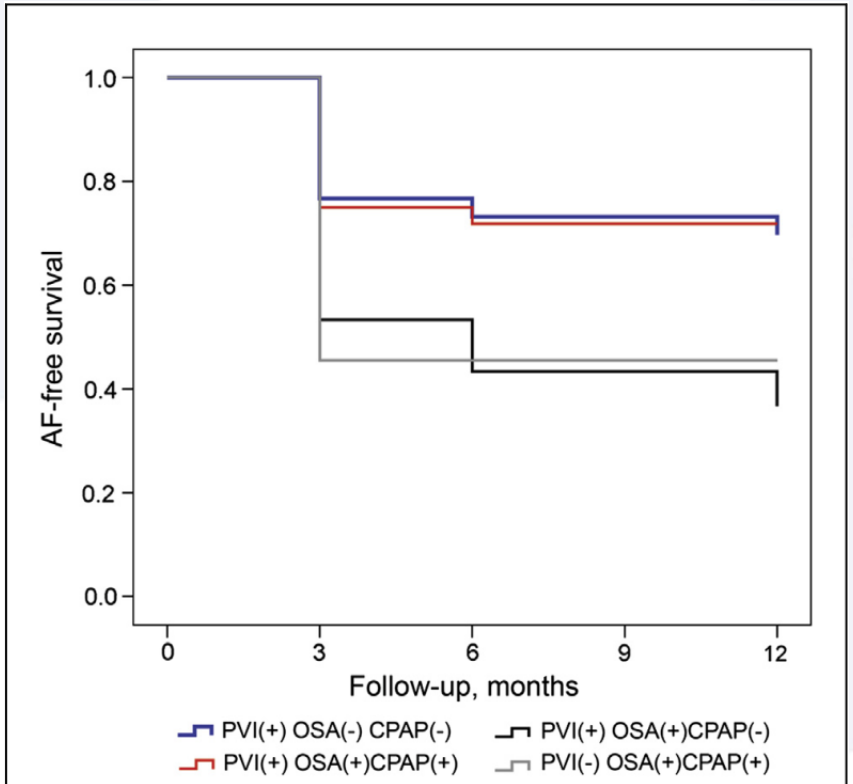


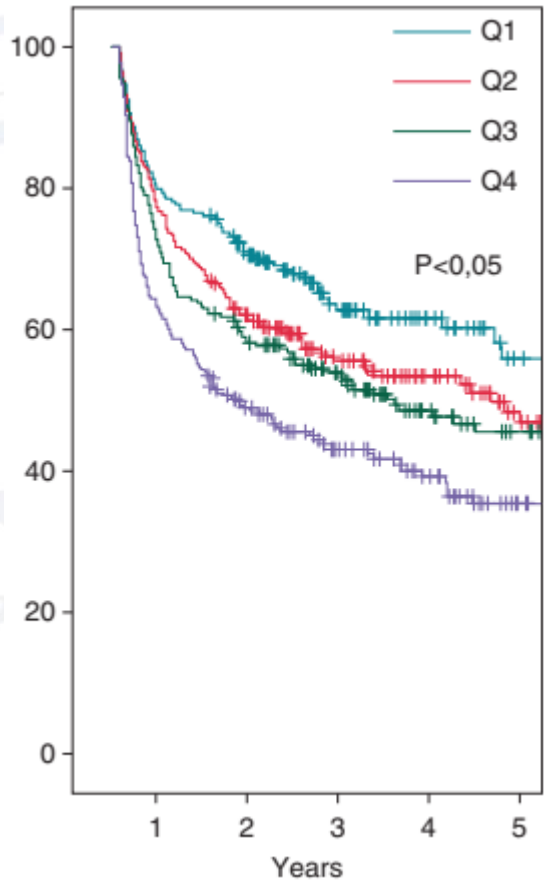
Figure 2 Kaplan-Meier Survival Curves According to Treatment Group

J Am Coll Cardiol. 2013 Jul 23;62(4):300-5

Ablación de la FA. Algo más que catéter.

HOSPITAL UNIVERSITARIO CENTRAL de ASTURIAS

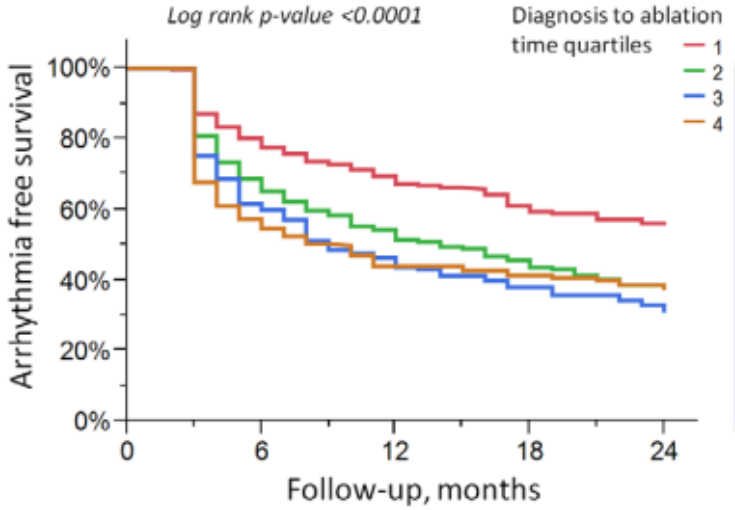
Diagnosis-to-ablation time as a predictor of success: early choice for pulmonary vein isolation and long-term outcome in atrial fibrillation: results from the Middelheim-PVI Registry

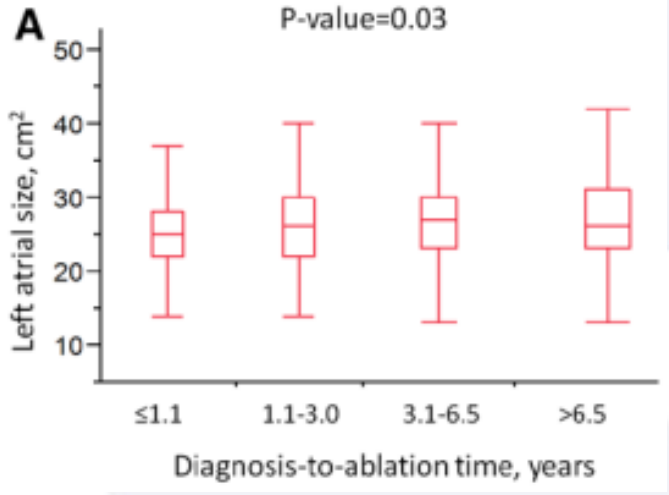


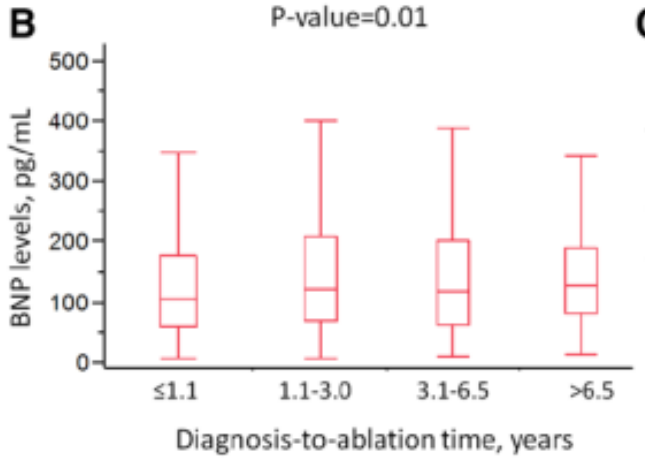
Europace. 2018 Apr 1;20(4):589-595

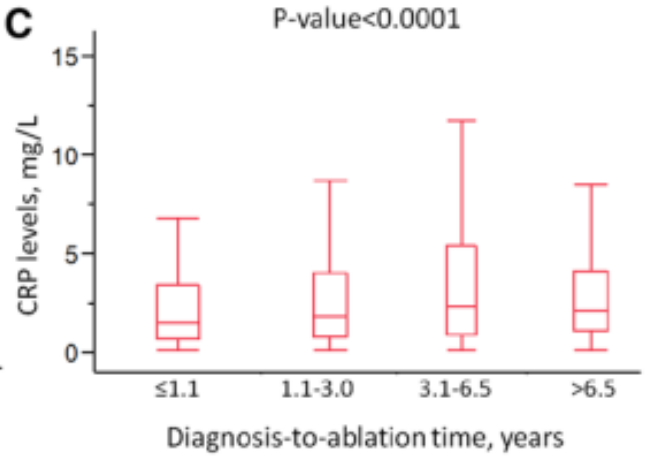
Radiofrequency Ablation of Persistent Atrial Fibrillation

Diagnosis-to-Ablation Time, Markers of Pathways of Atrial Remodeling, and Outcomes









Circ Arrhythm Electrophysiol. 2016;9:e003669

Con una visión integral parece que estamos mejorando!!!!

HOSPITAL UNIVERSITARIO CENTRAL de ASTURIAS

Temporal trends in atrial fibrillation recurrence rates after ablation between 2005 and 2014: a nationwide Danish cohort study

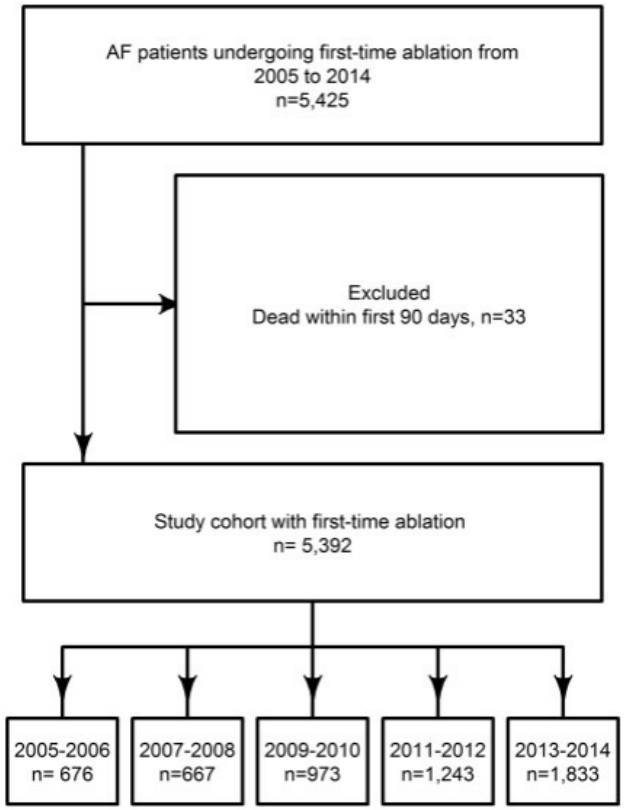


Figure 1 Flowchart of patient inclusion. AF, atrial fibrillation.

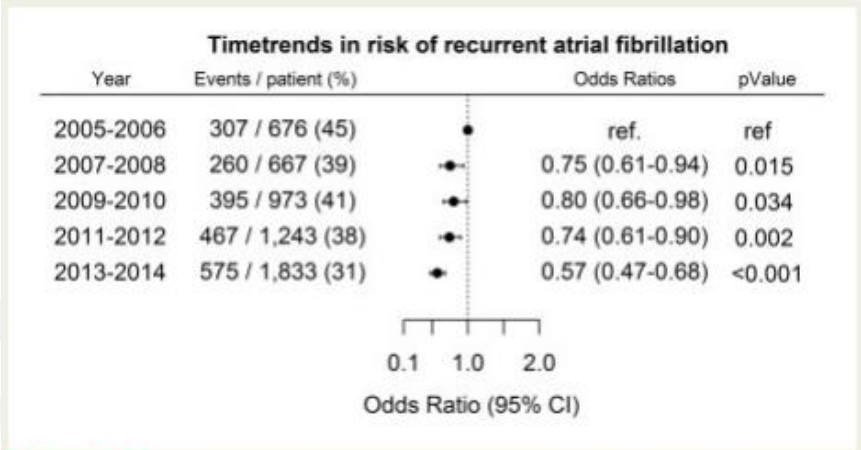
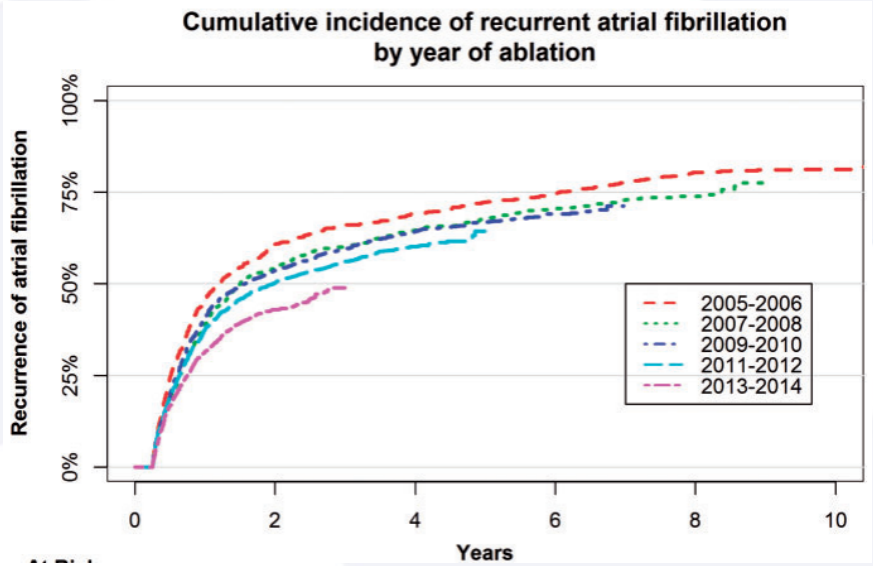


Figure 2 Time trends in recurrent atrial fibrillation 1 year after first time ablation. Adjusted for age, sex, duration of atrial fibrillation, hypertension, heart failure, diabetes mellitus, vascular disease, chronic kidney disease, cardioversion 1 year prior to ablation. CI, confidence interval.



Eur Heart J. 2018 Feb 7;39(6):442-449

- ***¿A quién?*** *Ajustando la indicación al perfil clínico del paciente.*

- ***¿Cuándo?*** *Una vez tomada la decisión estratégica….. cuanto antes.*

- ***¿Cómo?*** *(1) Procurando un aislamiento efectivo y duradero de las Venas Pulmonares. (2) Considerando técnicas adicionales en sustratos más complejos. (3) Y sin olvidar un manejo clínico integral y un control exhaustivo de los FRCV.*

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- David Testa (Biosense Webster).
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- Fco. Javier de Cos Juez.