Cardiomyopathie atriale

Est-il trop tard pour une ablation ?

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University of Pennsylvania

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Male, born in 1959, HTN, obesity, dilated cardiomyopathy (LVEF 30%)
2011: typical flutter ablation
2015 (age 56): paroxysmal AF with heart failure: CPVI

2016: recurrence
(persistent AF and AT),
new procedure:

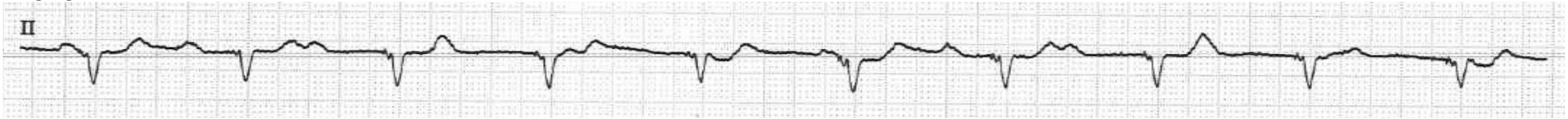
- RA map: 286 cc
- LA map: 291 cc
- DCC needed

2016: AF/AT recurrence

↓ *rate control decided*

Was this the good decision ?

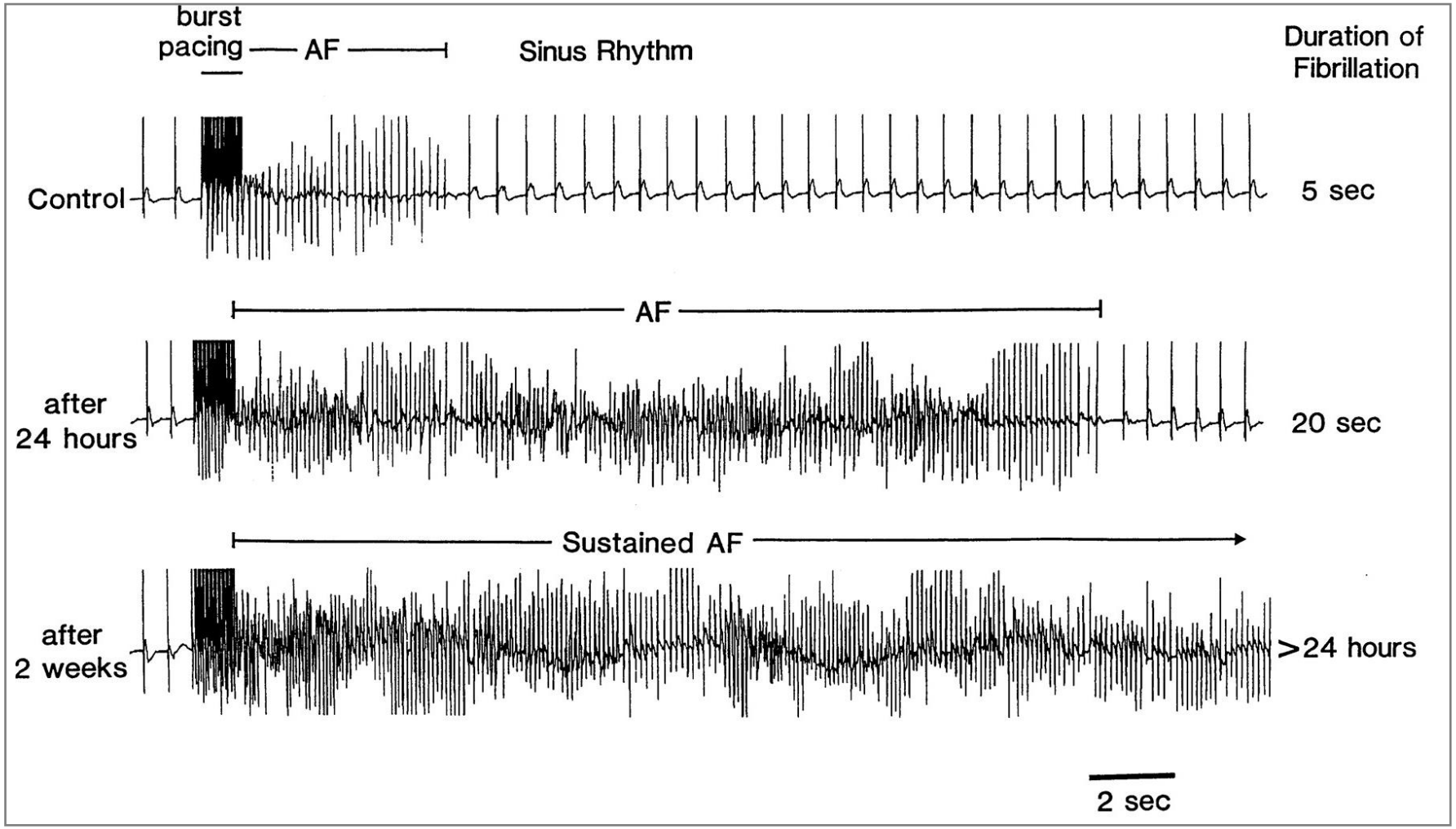
2016: AVN ablation + CRT-D (biventricular, no atrial lead)
2019: - 20kg
2020:

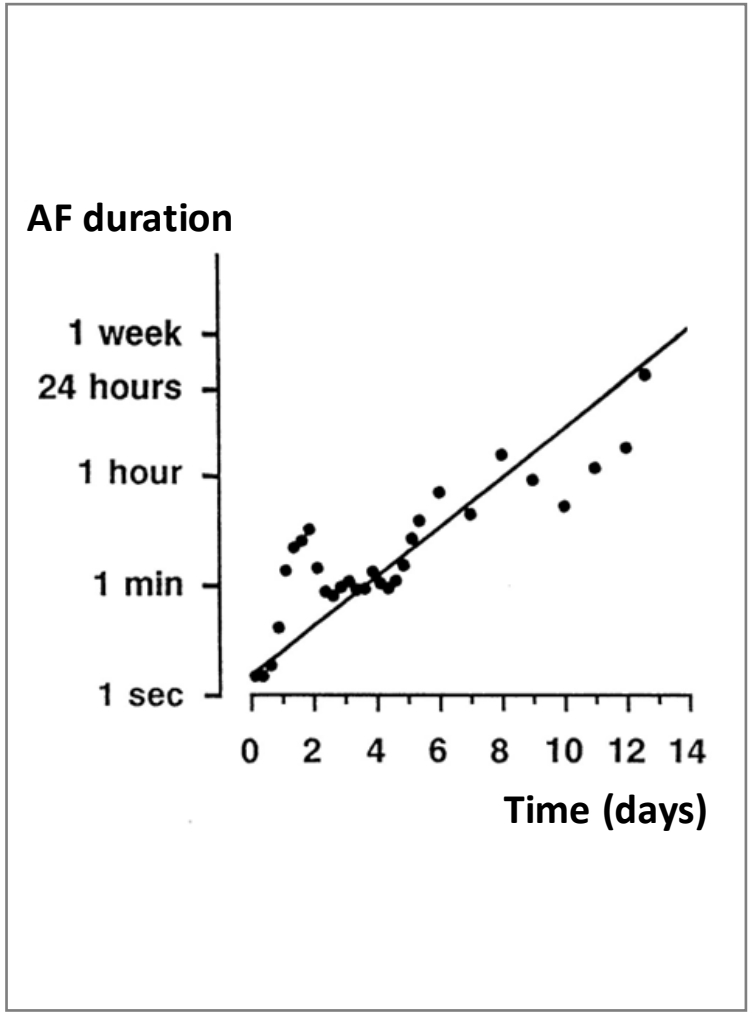


March 2024: atrial lead added, device change

12 goats, fibrillation pacemaker which artificially maintained AF

artificial maintenance of AF resulted in a progressive logarithmic increase in the duration of AF

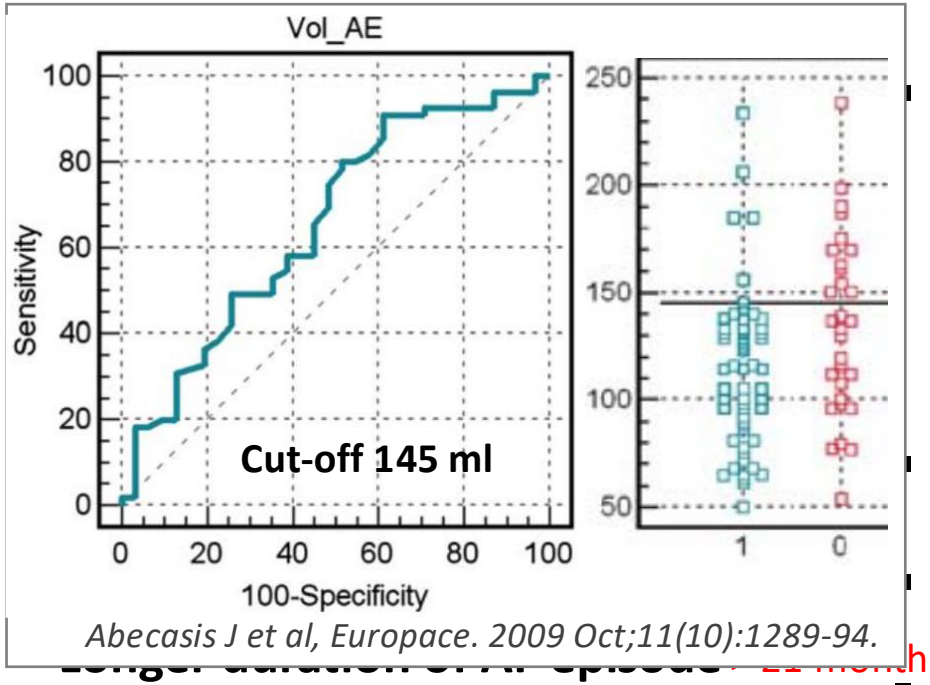




M C Wijffels, C J Kirchhof, R Dorland, M A Allessie, Circulation 1995 Oct 1;92(7):1954-68.

"Old-fashioned" predictors ?

- **LA Size** Φ > 50 mm, Volume > 126 ml (CT)
  - Neumann et al. Europace 2013 ;15(8) :1143-9.
  - Miyazaki et al. J Cardiovasc Electrophysiol. 2011;22(6):621-5.
  - Arya et al. Europace. 2010;12(2):173-80.



Abecasis J et al, Europace. 2009 Oct;11(10):1289-94.

Longer duration of AF episode > 21 months
  - Mulder et al. Europace 2012;14(6):818-25
  - Matsuo et al. J Am Coll Cardiol. 2009;54(9):788-95

- **Prior failure of procedure**
  - Khaykin Y et al. J Cardiovasc Electrophysiol. 2011;22(11):1206-14.

- $CHADS_2$ and/or **CHA_2DS_2-VASc**
  - Chao et al. Heart Rhythm 2012;9(8):1185-91
  - Letsas et al. Europace 2013 Epub
- **ECG cycle length** < 142 ms
  - Matsuo et al. J Am Coll Cardiol. 2009;54(9):788-95
- **ECG amplitude** of fibrillatory waves < 0.07 mV
  - Zarzoso V, Latcu DG et al, Arch Cardiovasc Dis. 2016 Dec;109(12):679-688.
  - Nault I, J Interv Card Electrophysiol. 2009 Oct;26(1):11-9.
  - Cheng et al. Ann Noninvasive Electrocardiol. 2013;18(4):352-8.
- **White blood cell count**
  - Letsas et al. Europace. 2009;11(2):158-63.
- **CRP**
  - Lellouche et al. Europace. 2009;11(5):662-4.
- **BMI**
  - Mainigi et al. J Cardiovasc Electrophysiol. 2007;18(1):69-74.
- **Sleep apnea**
  - Sauer et al. Heart Rhythm. 2006;3(9):1024-8.
  - Jongnarangsin et al. J Cardiovasc Electrophysiol. 2008; 19(7):668-72.
- **Renal function**
  - Chao et al. Circ J. 2011;75(10):2326-32.

- **Hypertension**
  - Arya et al. Europace. 2010;12(2):173-80.
  - Khaykin Y et al. J Cardiovasc Electrophysiol. 2011; 22(11):1206-14.
  - Letsas et al. Europace. 2009;11(2):158-63.
- **MRI fibrosis** TTE: LA strain
  - *Marrouche NF, JAMA 2014;311(5):498-506.*
  - den Uijl et al. Heart. 2011;97(22):1847-51.
- **Initial voltage map (fibrosis)**
- **Strain and Strain rate**
  - Schneider et al. Eur Heart J. 2008;29(11):1397-409.
  - Hammerstingl et al. J Cardiovasc Electrophysiol. 2012;23(3):247-55.
- **Atrial conduction time** P-Aa > 130 ms
  - den Uijl et al. Europace. 2011; 13(11):1533-40.
- **Left atrial appendage peak velocity** – transesophageal echocardiography < 0.3 m/s
  - Combes et al. Arch Cardiovasc Dis. 2013;106(1):36-43.

Plan

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ESC European Society of Cardiology

EHRA DOCUMENT

EHRA European Heart Rhythm Association

Atrial cardiomyopathy revisited—evolution of a concept: a clinical consensus statement of the European Heart Rhythm Association (EHRA) of the ESC, the Heart Rhythm Society (HRS), the Asian Pacific Heart Rhythm Society (APHRS), and the Latin American Heart Rhythm Society (LAHRS)

Andreas Goette, Domenico Corradi, Dobromir Dobrev, Luis Aguinaga, Jose-Angel Cabrera, Sumeet S. Chugh, Joris R. de Groot, Laurie Soulat-Dufour, Guilherme Fenelon, Stephane N. Hatem, Jose Jalife, Yenn-Jiang Lin, Gregory Y.H. Lip, Gregory M. Marcus, Katherine T. Murray, Hui-Nam Pak, Ulrich Schotten, Naohiko Takahashi, Takanori Yamaguchi, William A. Zoghbi, and Stanley Nattel

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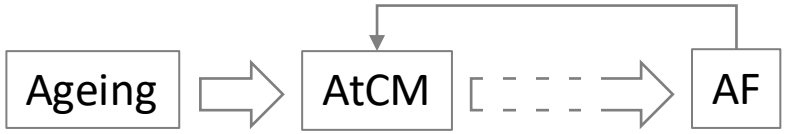
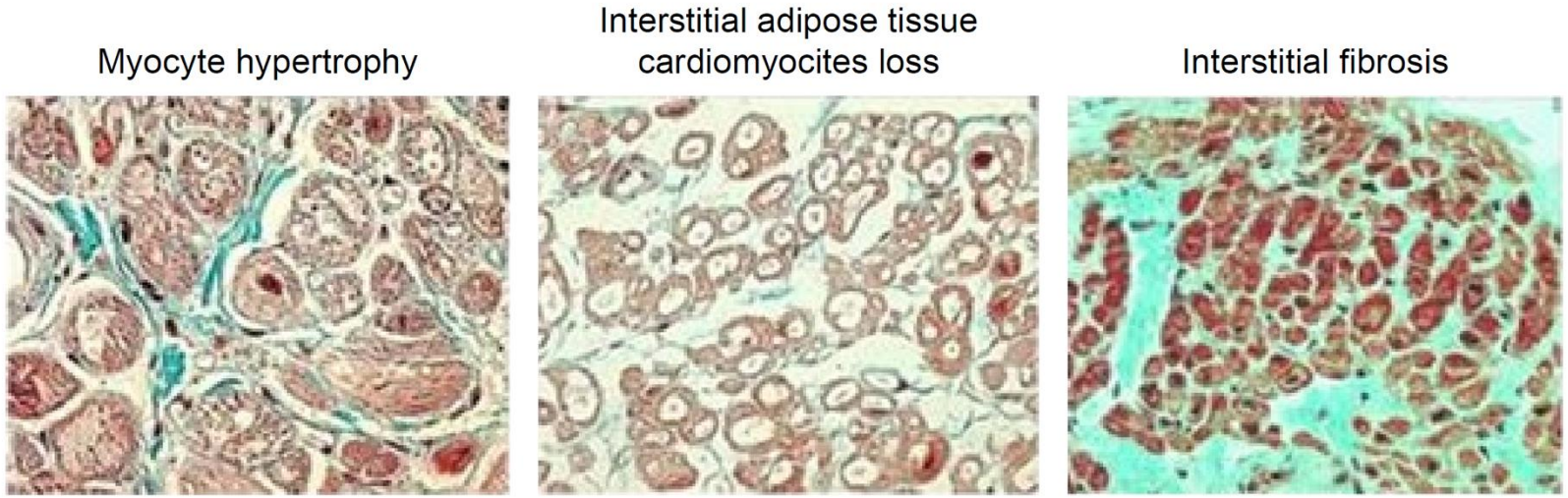
Atrial cardiomyopathy (AtCM):

Any complex of structural, architectural, contractile or electrophysiological changes affecting the atria with the potential to produce clinically relevant manifestations:

AtCM ⇄ AF

- atrial arrhythmia (e.g. atrial fibrillation (AF) and atrial flutter)
- atrial thrombogenesis
- atrial failure
- atrio-ventricular valve dysfunction secondary to atrial dilation

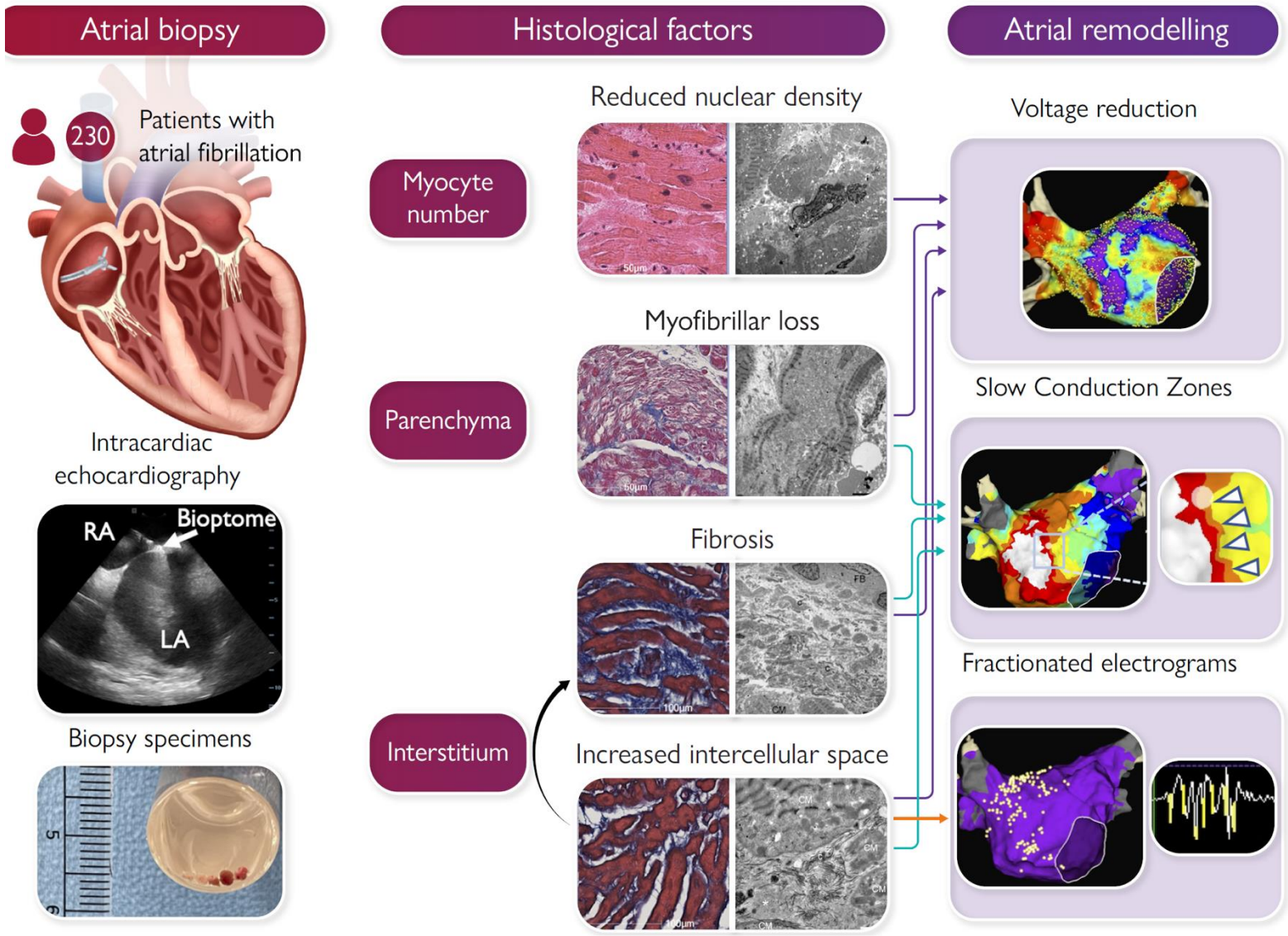


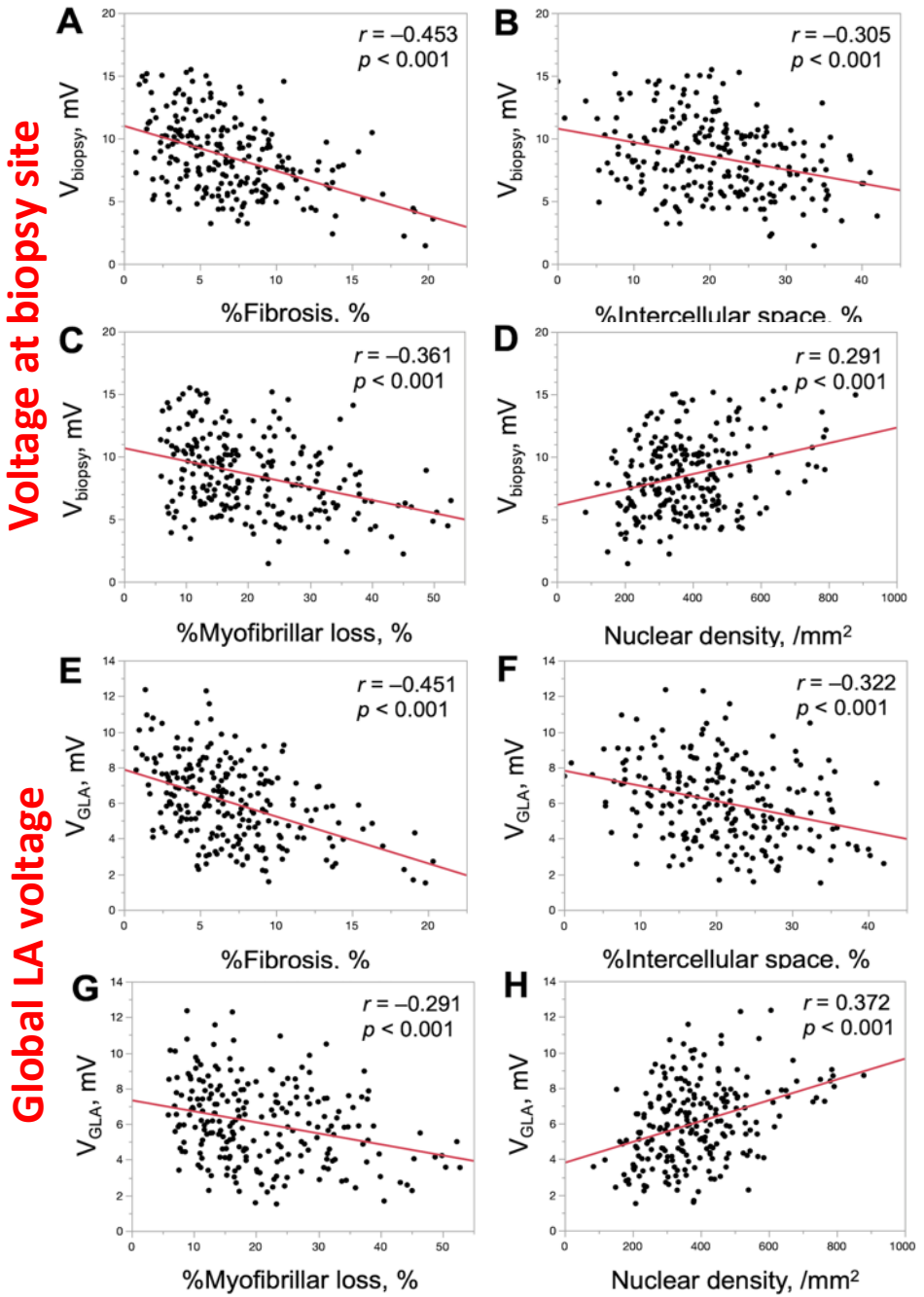


Masson's trichrome staining

Goette A et al, Europace 2024 Aug 30;26(9):euae204.

- 230 patients: AF ablation and endomyocardial atrial biopsy





Takahashi Y. et al, Eur Heart J 2023;44:3339–53.

Gender differences in atrial cardiomyopathy

Meta-analysis: 19 studies (151 370 patients; 34% women): women → lower efficacy and a higher risk of complications

Cheng X et al, Europace 2019;21:1509–18.

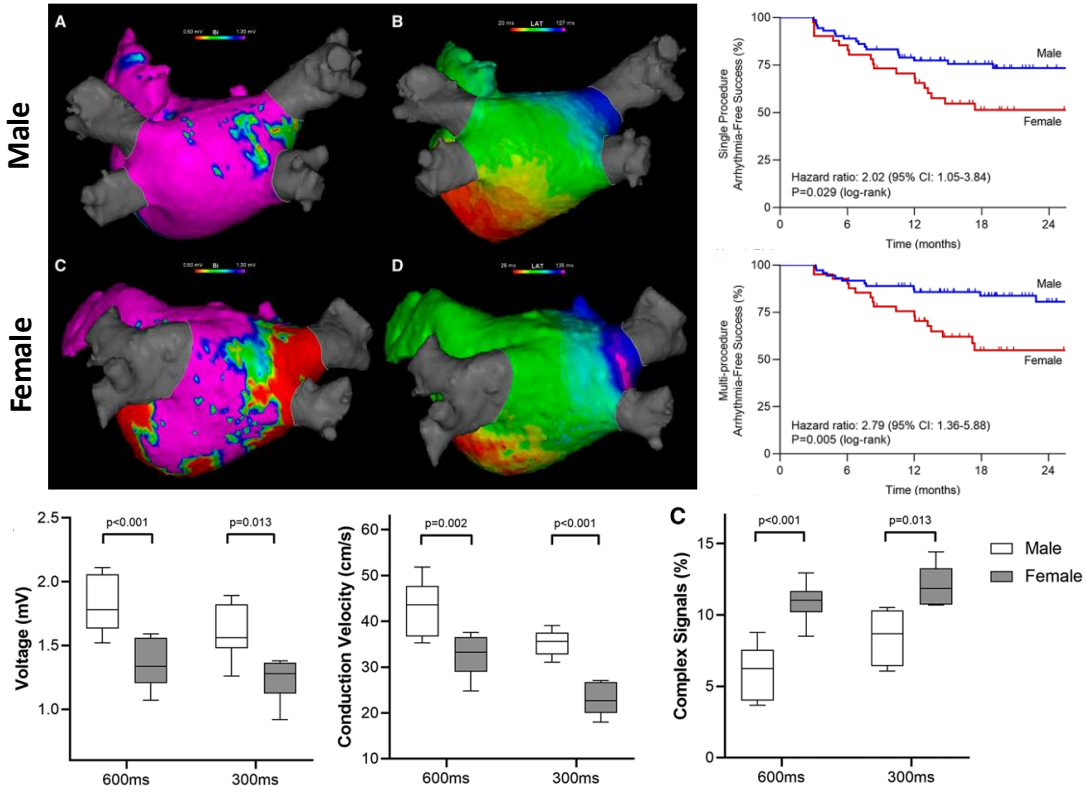
Predictors of atrial enhancement (MRI) in AF patients

Multivariate Analysis	Standardized β	Partial R^2	*P*
Female Gender	0.382	0.136	0.002
AF persistence	0.311	0.097	0.009

Cochet H et al, J Cardiovasc Electrophysiol 2015;26:484–92.

- 116 (42 female) consecutive patients with AF

≈ 50% paroxysmal, HD map in CS pacing, PVI in all

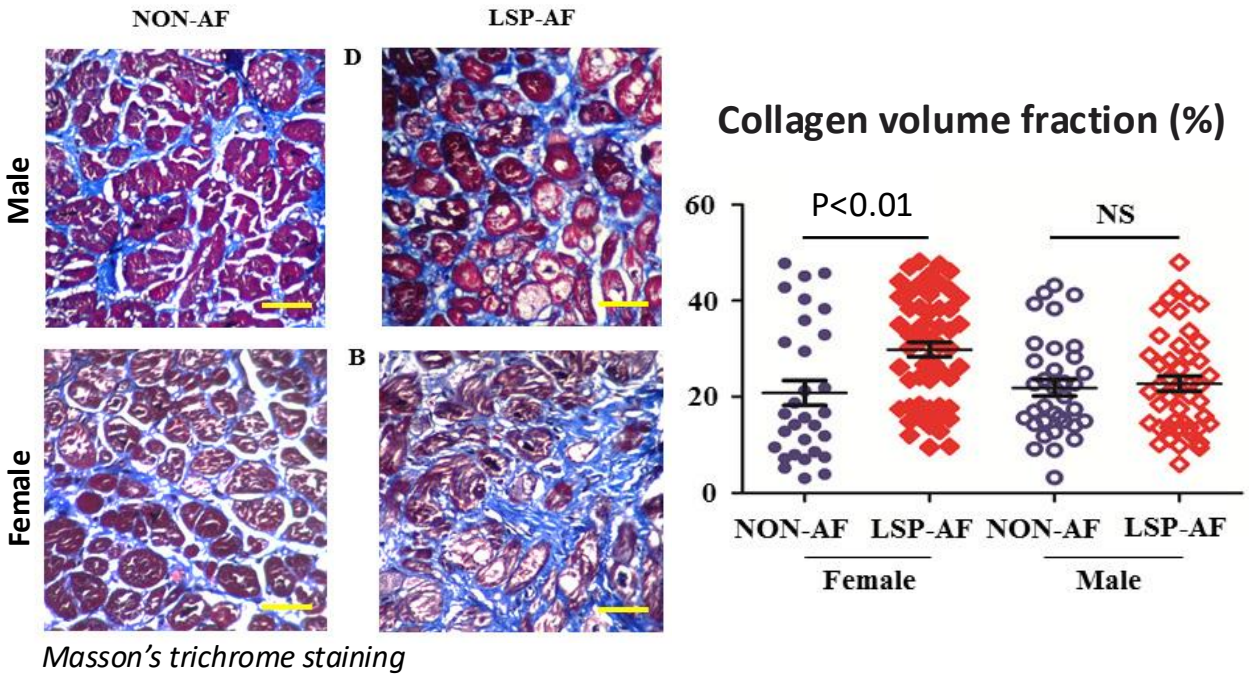


Female sex and **persistent AF** = independent predictors of single / multiprocedure arrhythmia recurrence (multivariable analysis)

Wong GR et al, Circ Arrhythm Electrophysiol 2022;15:e009925.

- 166 patients with dilated LA + mitral valve surgery:

PV vein sleeves (1 cm away from right PV orifices)



Masson's trichrome staining

Immunohistochemistry and microarray analysis: differential expression of fibrosis related genes and proteins:

→ the TGFβ/Smad3 pathway up-regulated in female LSP-AF group suggesting the aggravation of fibrosis remodeling.

Li Z et al, Oncotarget 2017;8: 53714–29.

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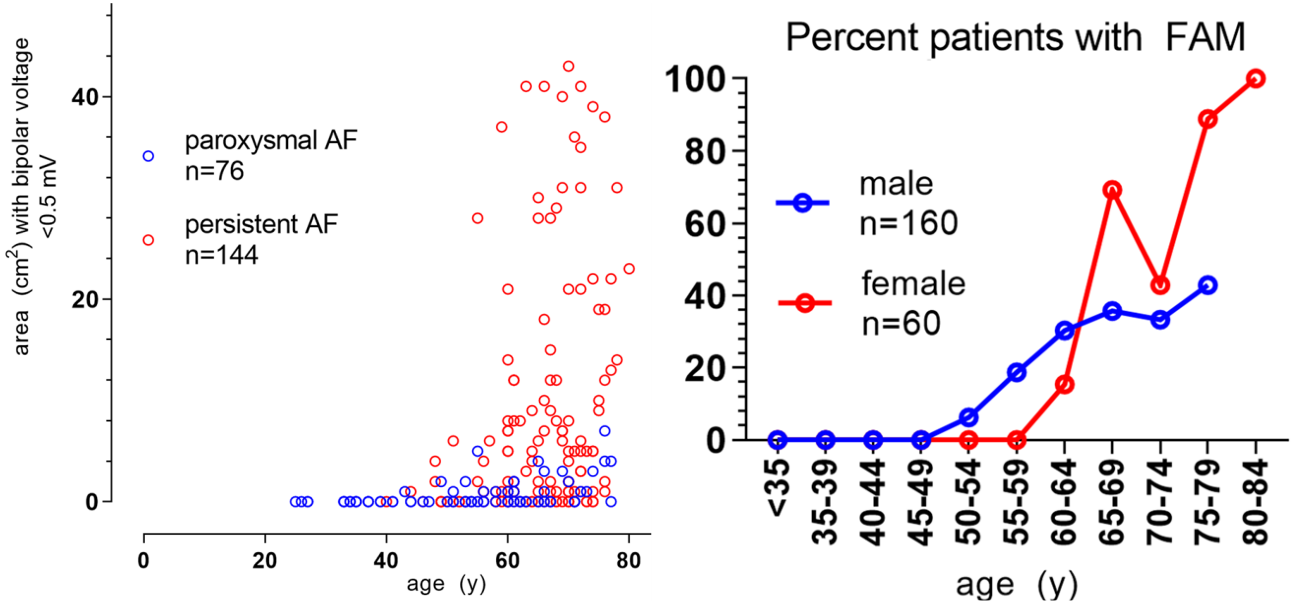
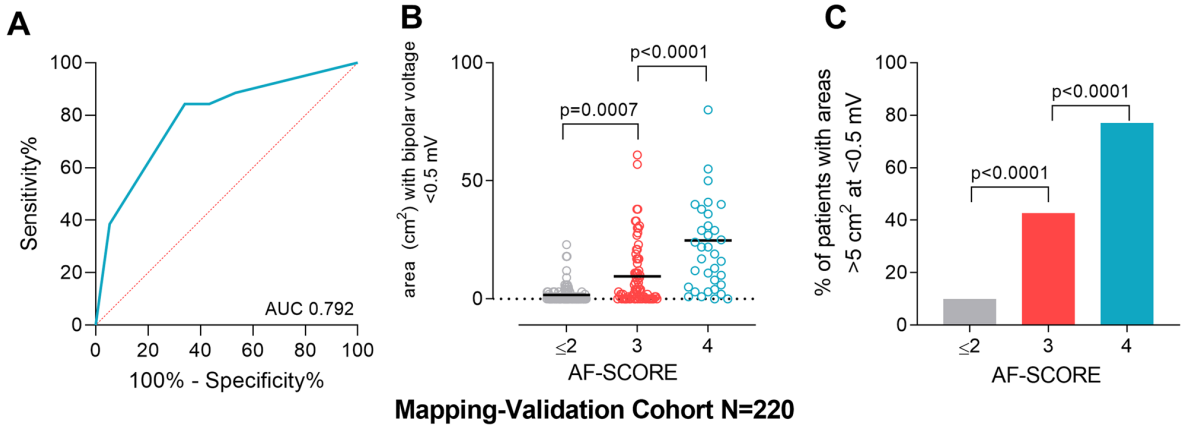
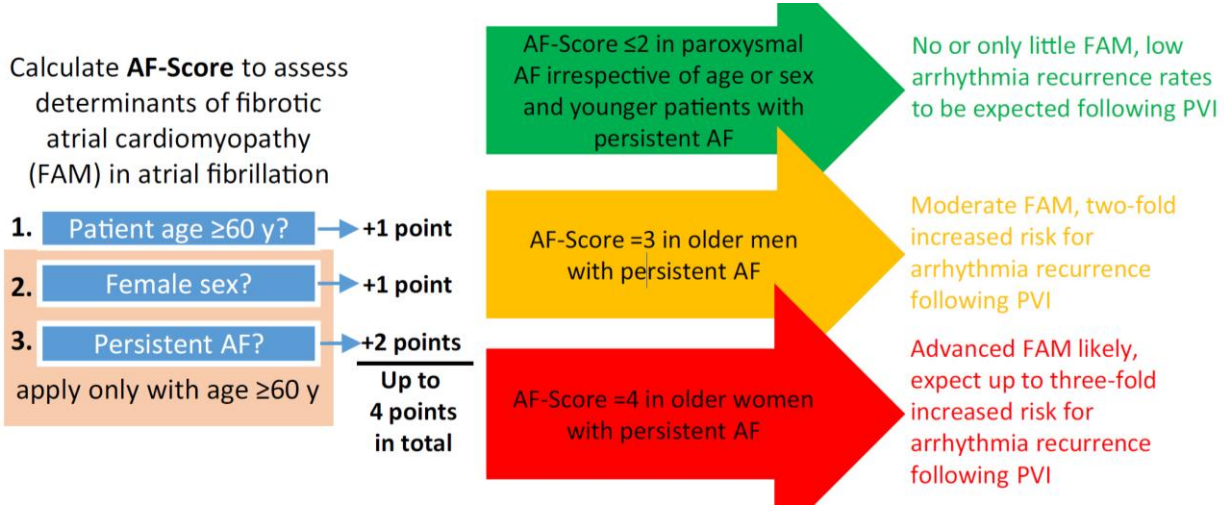
Predicting atrial cardiomyopathy (AF-Score)

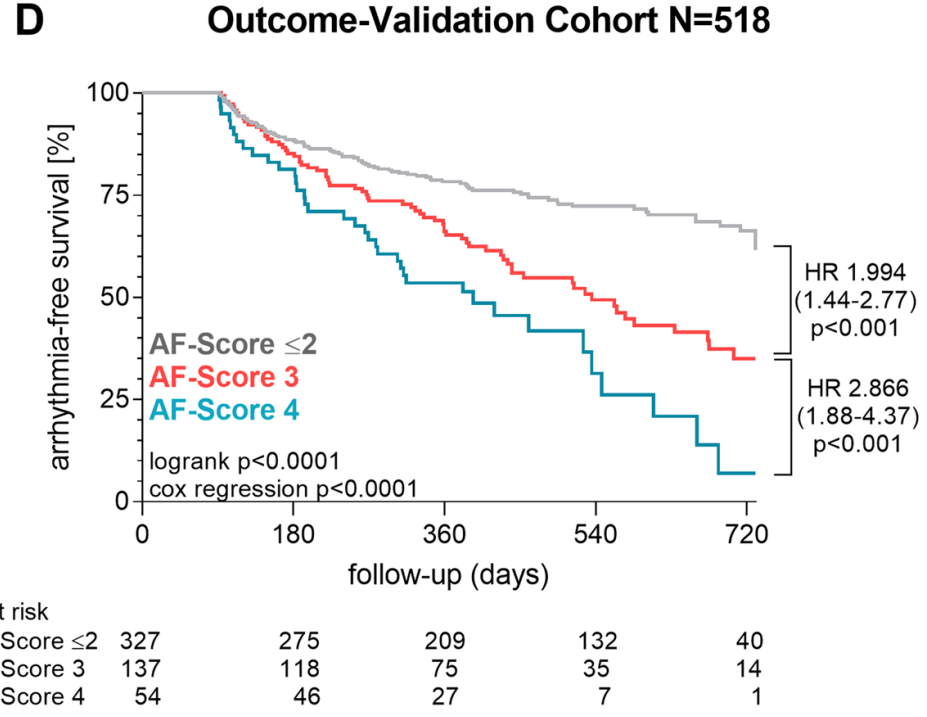
- 220 patients (73% male) undergoing high-density left-atrial(LA) voltage-mapping in SR; low-voltage < 0.5 mV bipolar EGM

Fibrotic atrial cardiomyopathy (FAM) = low voltage > 5 cm²









Müller-Edenborn B et al (RETAC), Clin Res Cardiol 2022;111:1018–27.

Predicting atrial cardiomyopathy (DR-FLASH)

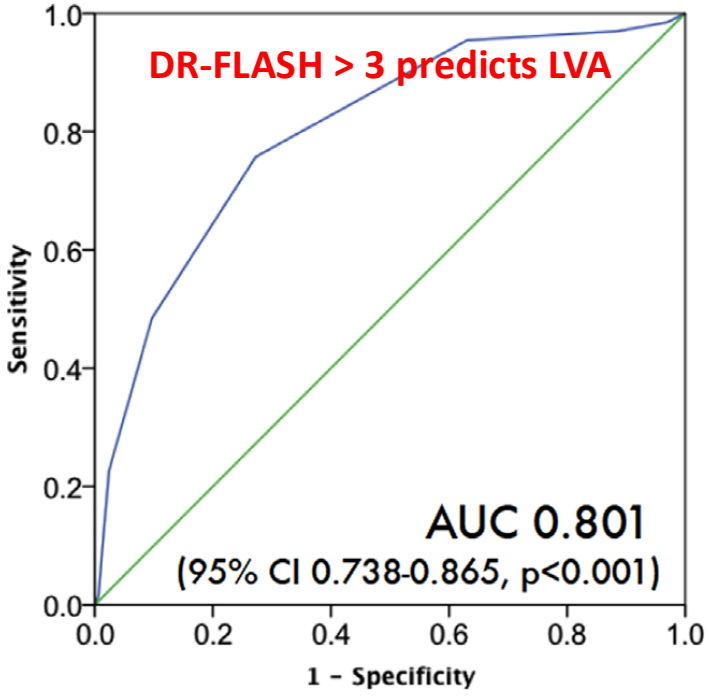
Kosiuk J et al, Heart Rhythm 2015;12:2207–2212.

DR-FLASH score (0÷7)
1 point each

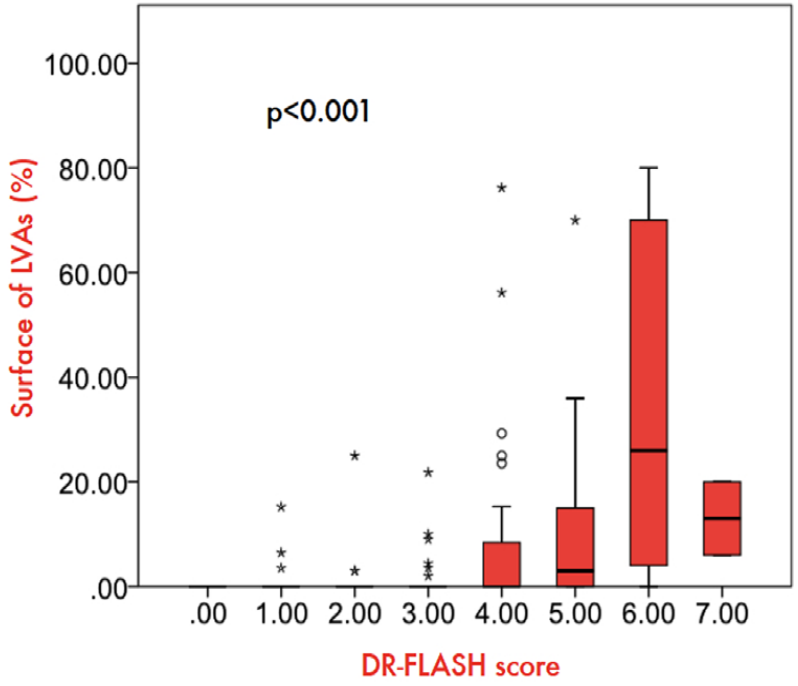
- diabetes mellitus
- renal dysfunction (eGFR < 90 ml/min/1.73m^2)
- persistent form of AF
- LA diameter > 45 mm
- Age > 65 years
- Female sex
- Hypertension

LVA (low-voltage areas) = at least 3 adjacent points < 0.5 mV (EAM in SR)

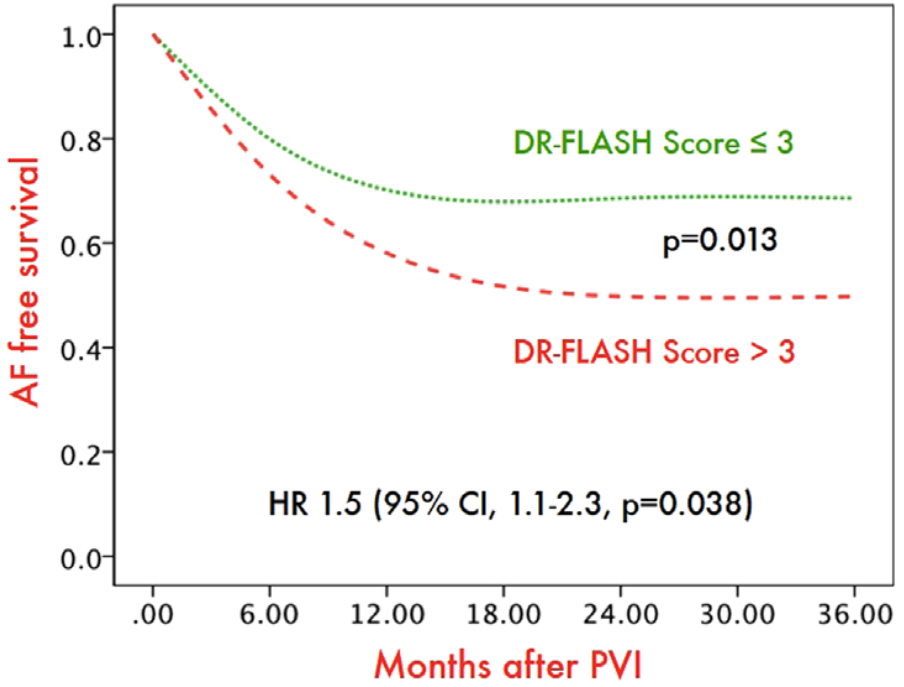
- 238 patients: basic cohort



- 180 patients: validation cohort



- 484 patients: PVI cohort



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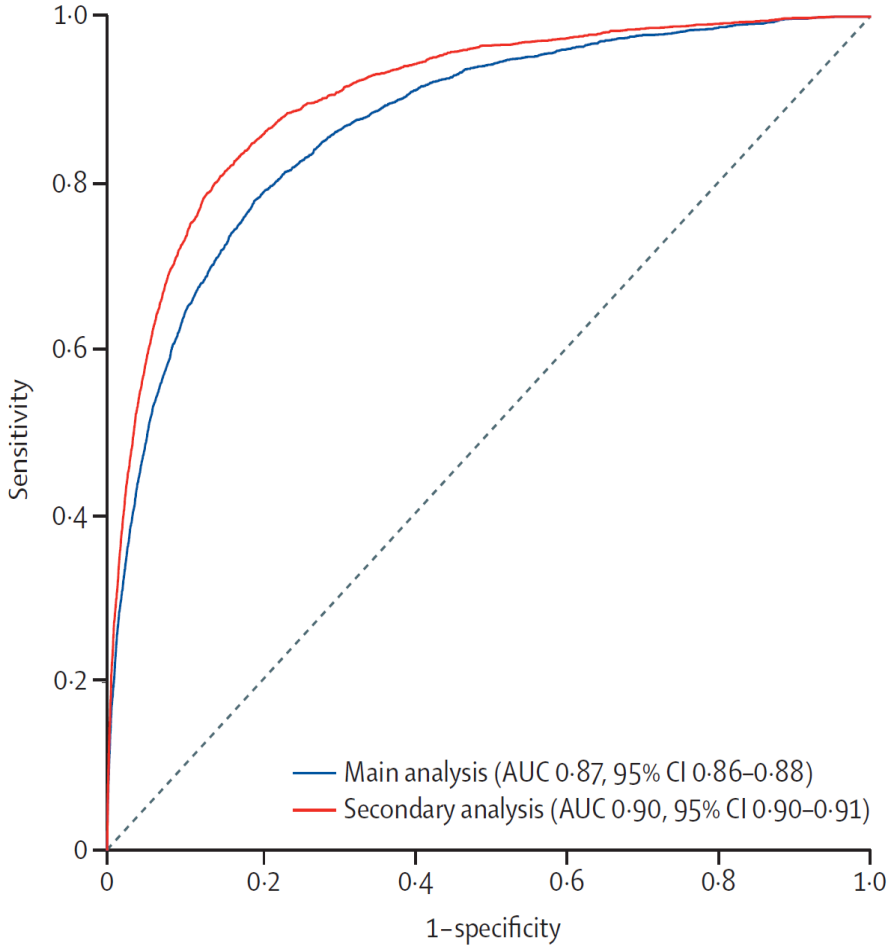
ECG abnormalities in AtCM

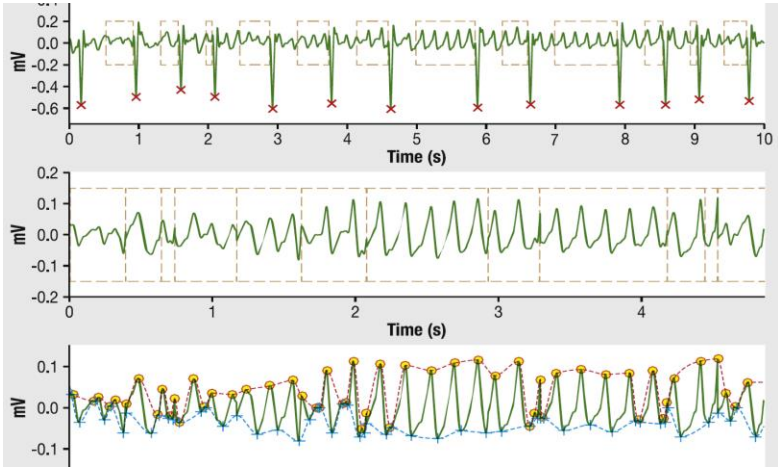
	Associations	References
Amplified digital p-wave duration (APWD)	Atrial fibrosis/low voltage	280,281
	Atrial contractile dysfunction, LAA thrombogenesis	120,221
	Reduced LAA-velocity	120
	AF	282
	AF recurrence after catheter ablation	280,281
PTFV1	Low LA appendage ejection velocity	283
	Functional atrial remodelling	284
	AF	285
	AF recurrence after catheter ablation	286
P-wave axis	AF	287
P-wave voltage	AF	288
	AF recurrence after catheter ablation	289
P-wave area	LA enlargement	290
	AF in mitral stenosis	291
P-wave dispersion	Idiopathic paroxysmal AF	292,293
	AF recurrence after cardioversion	294
Fibrillatory wave (F-wave)	LA enlargement	295–297
	Low LA appendage flow	296
	Long-standing persistent AF	297,298
	Heart failure	297
	AF recurrence after catheter ablation	299,300

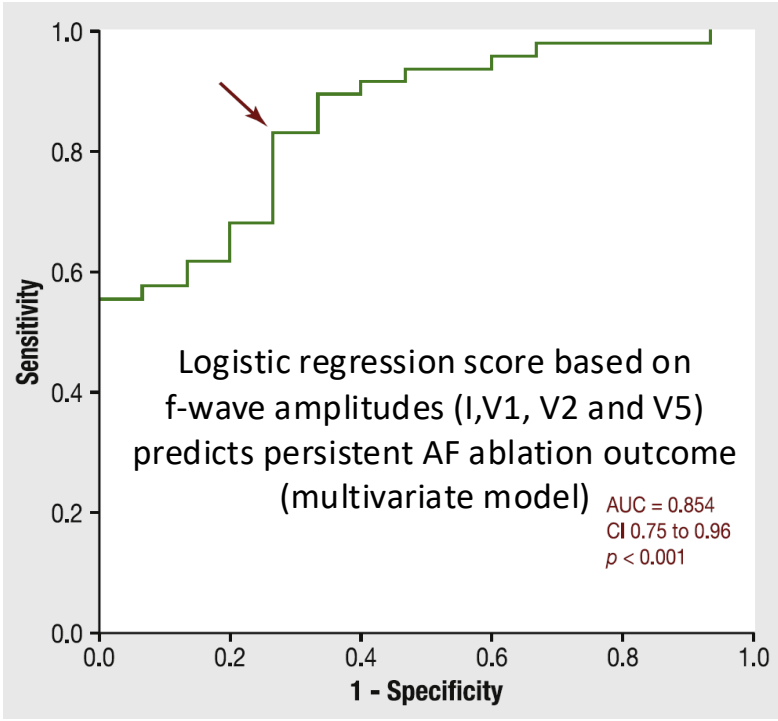
Goette A et al, Europace 2024 Aug 30;26(9):euae204.

AI-enabled ECG in SR identifies individuals with AF



Attia ZI et al, Lancet 2019;394:861–7.





Zarzoso V, Latcu DG et al, Archives of Cardiovascular Disease (2016) 109, 679—688

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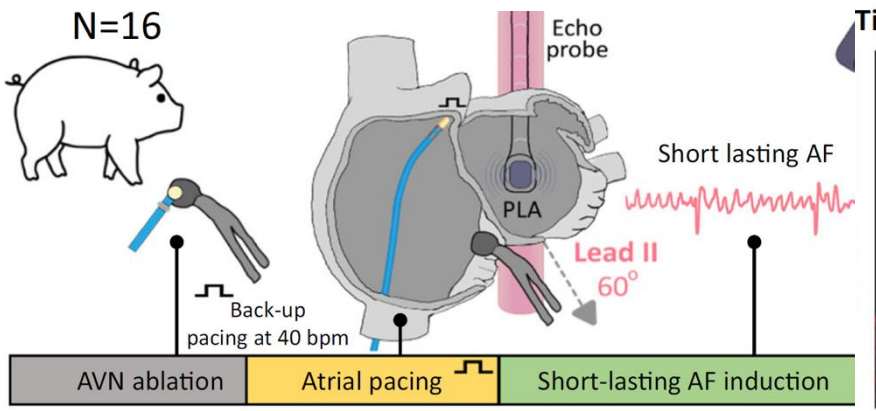
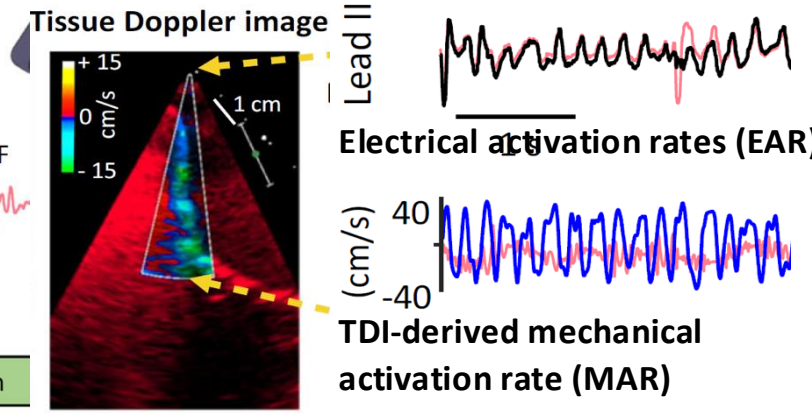
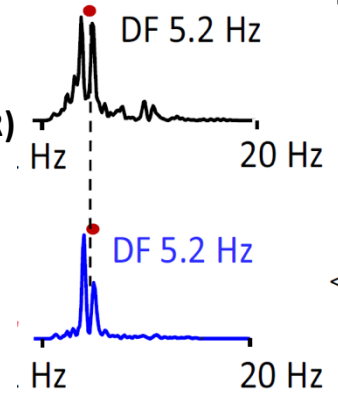
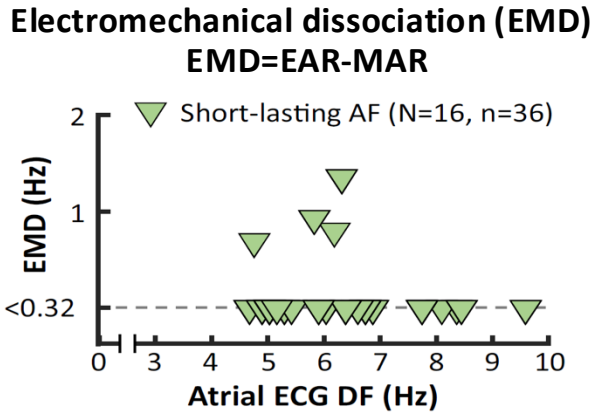
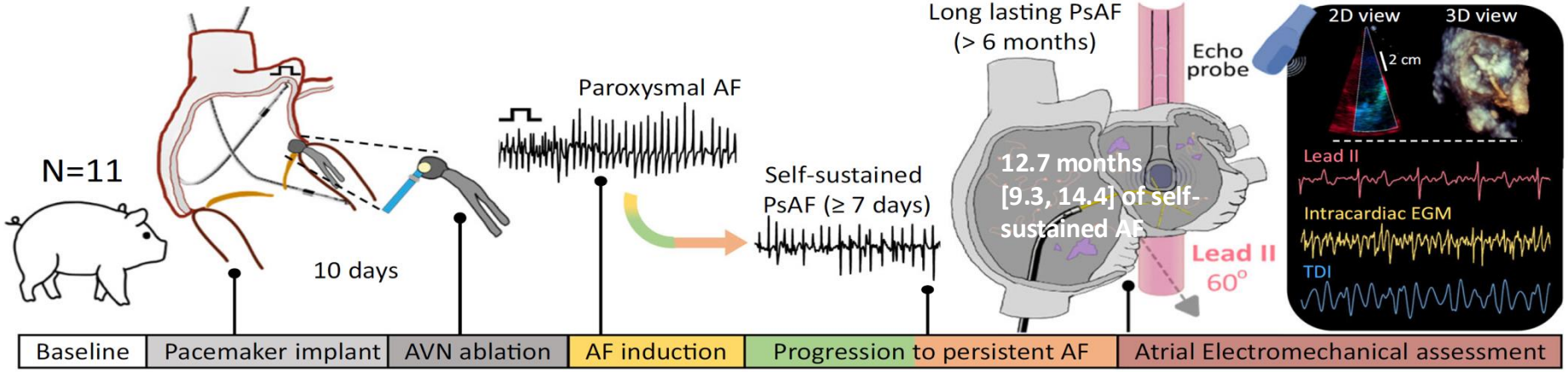
Atrial electro-mechanical dissociation

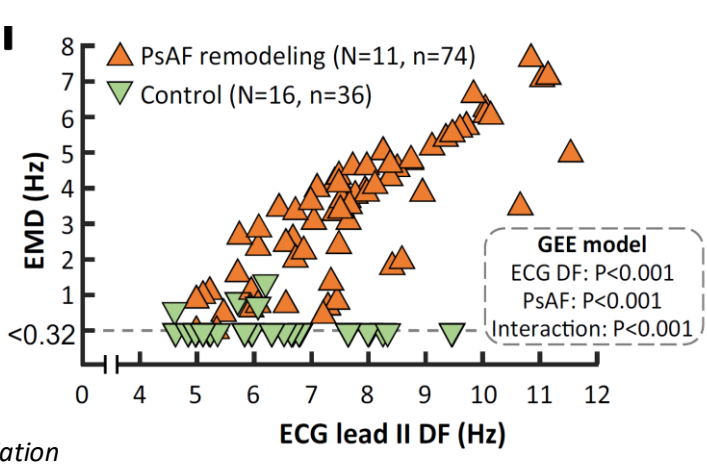






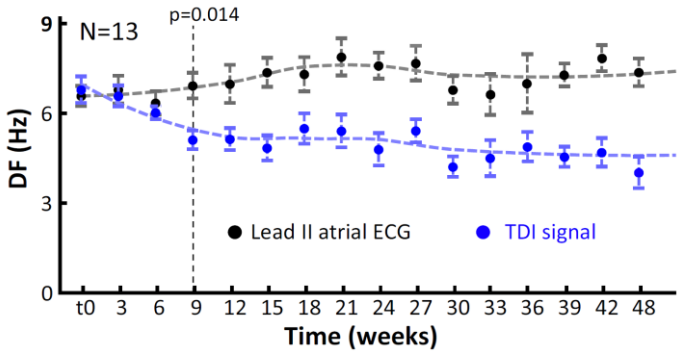


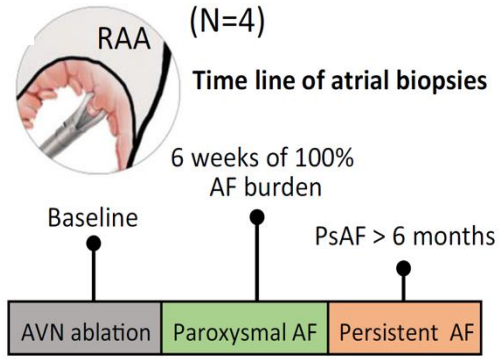


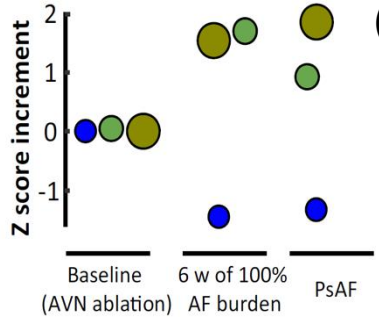


After 27.0 months [24.4, 35.7] of protocol initiation

N=13 **EMD is progressive** (TEE+ECG every 3 weeks)





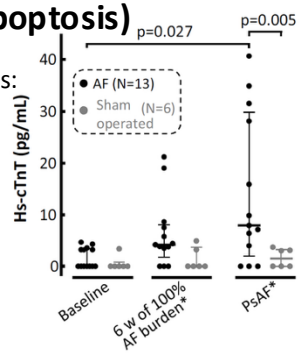


Fibrotic and contractile remodeling

Atrial myocardial damage during AF (biomarkers of apoptosis)

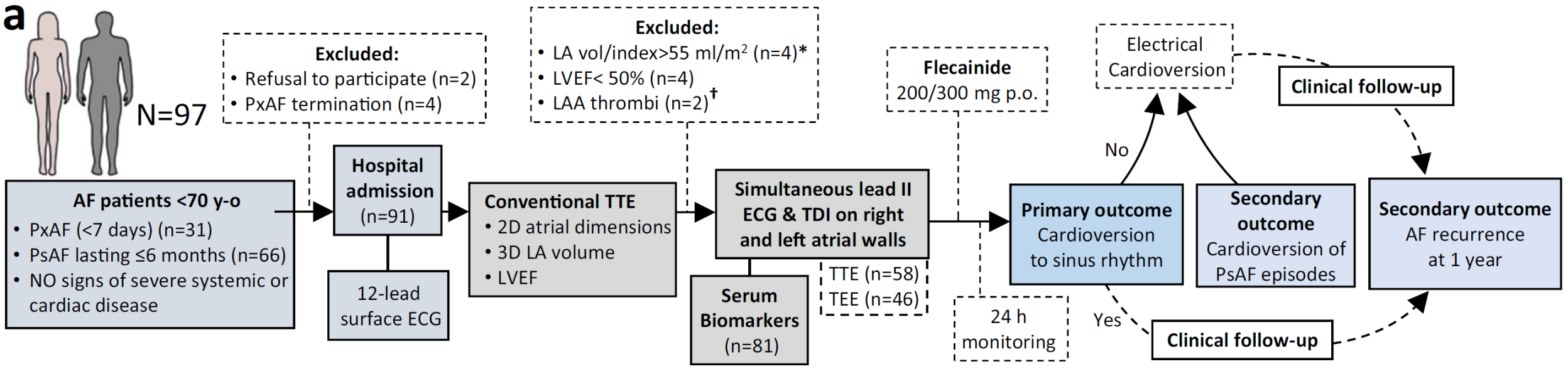
↗ in LA of PsAF animals:
- Caspase 3⁺ nuclei
- TUNEL⁺ nuclei
- BAX protein

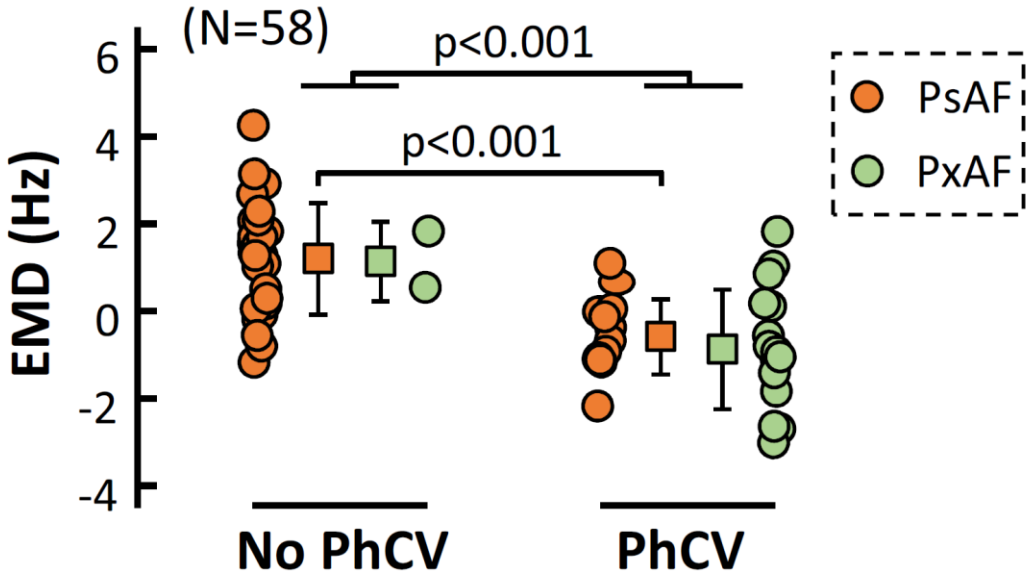
Muscle contraction
Collagen-containing ECM
ECM structural resistance

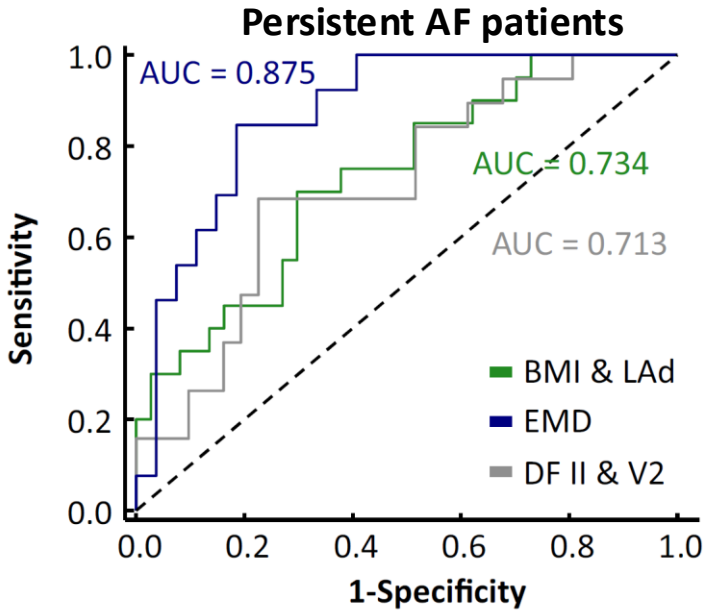


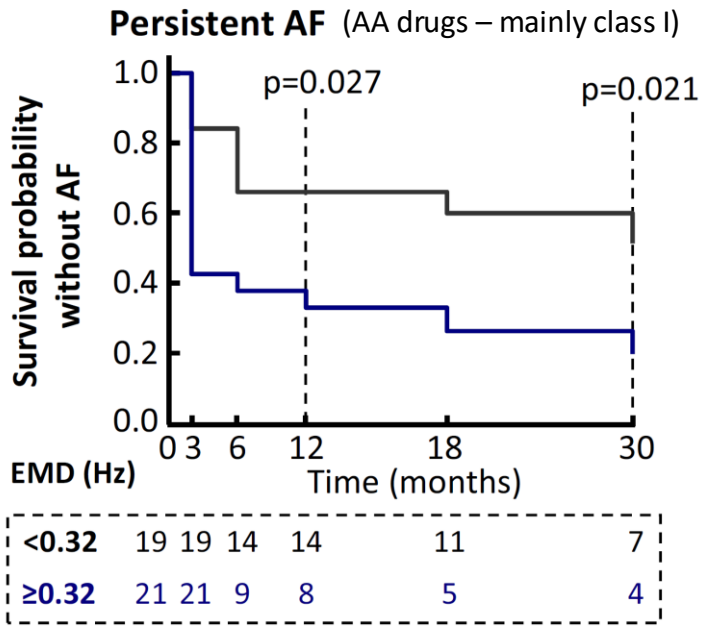
Optical mapping (ex-vivo): **AF remodeling affects calcium dynamics,** which may exacerbate EMD in vivo

Atrial electro-mechanical dissociation









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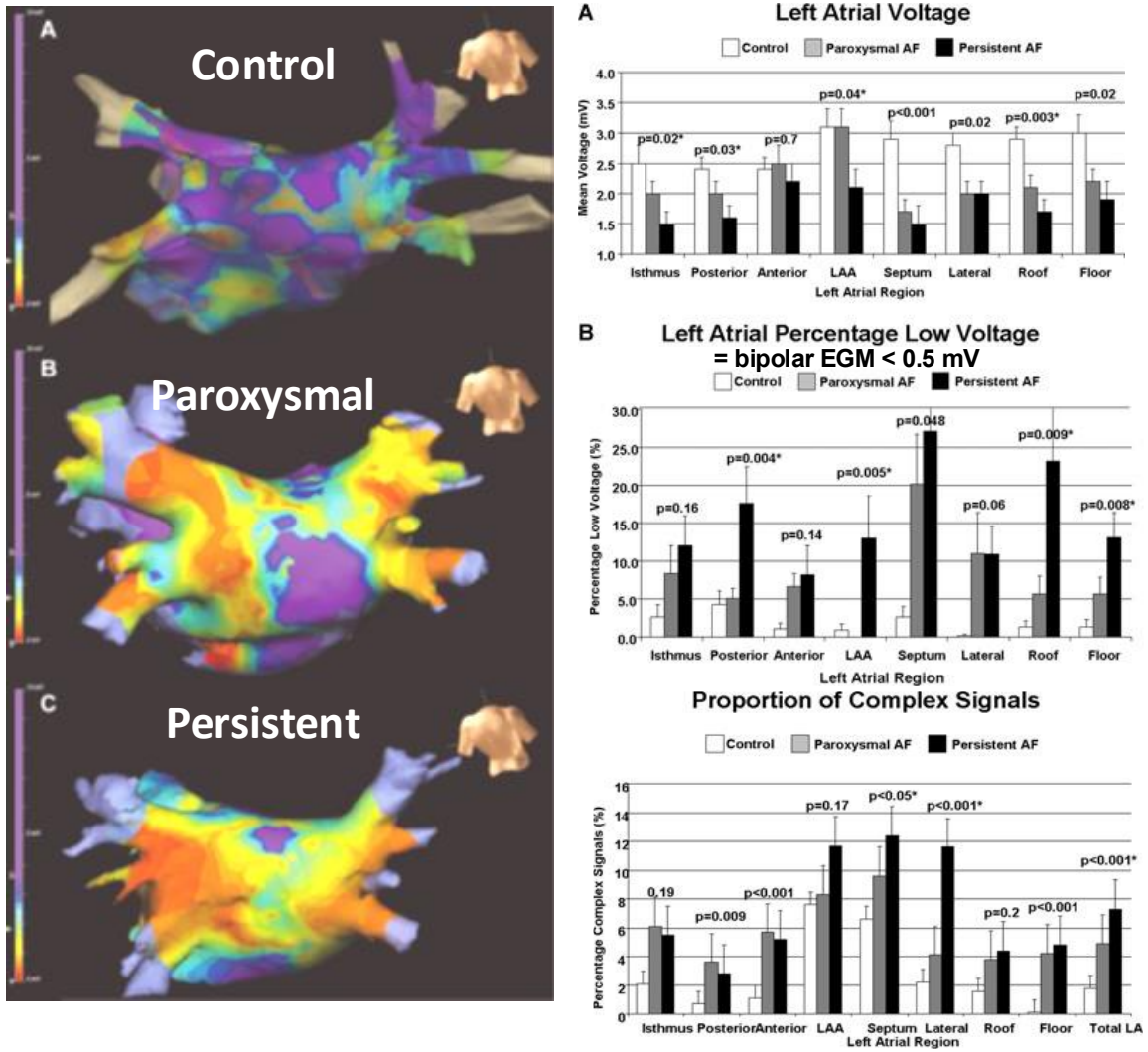
6. Atrial electro-mechanical dissociation
7. **Electro-anatomical mapping**
8. SR maintains SR

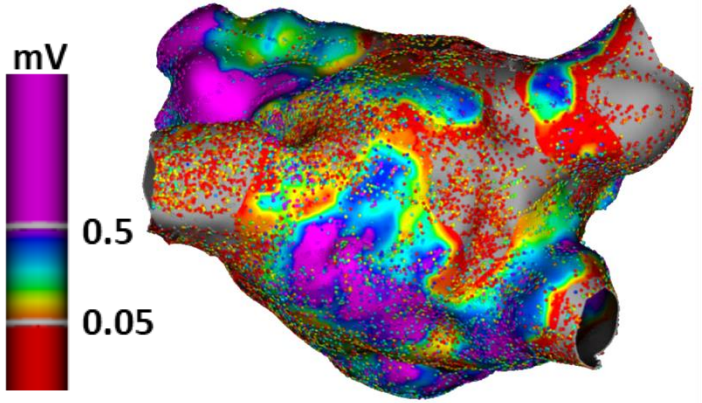
N=46 Complex signals during SR =

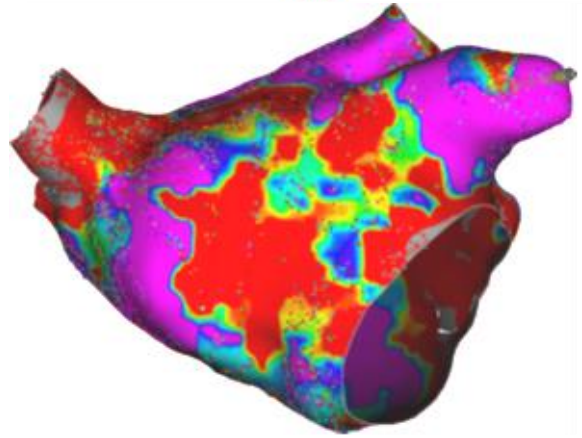
- ≥3 deflections >50 ms duration or
- 2 separate deflections separated by an isoelectric interval

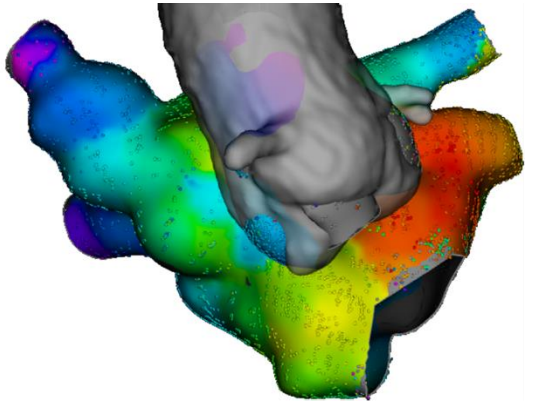
Voltage and activation maps CSd pacing 600 ms

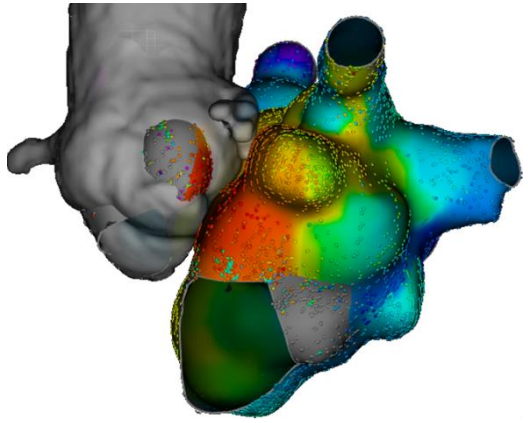


Teh AW et al, J Cardiovasc Electrophysiol 2012;23:232–8.







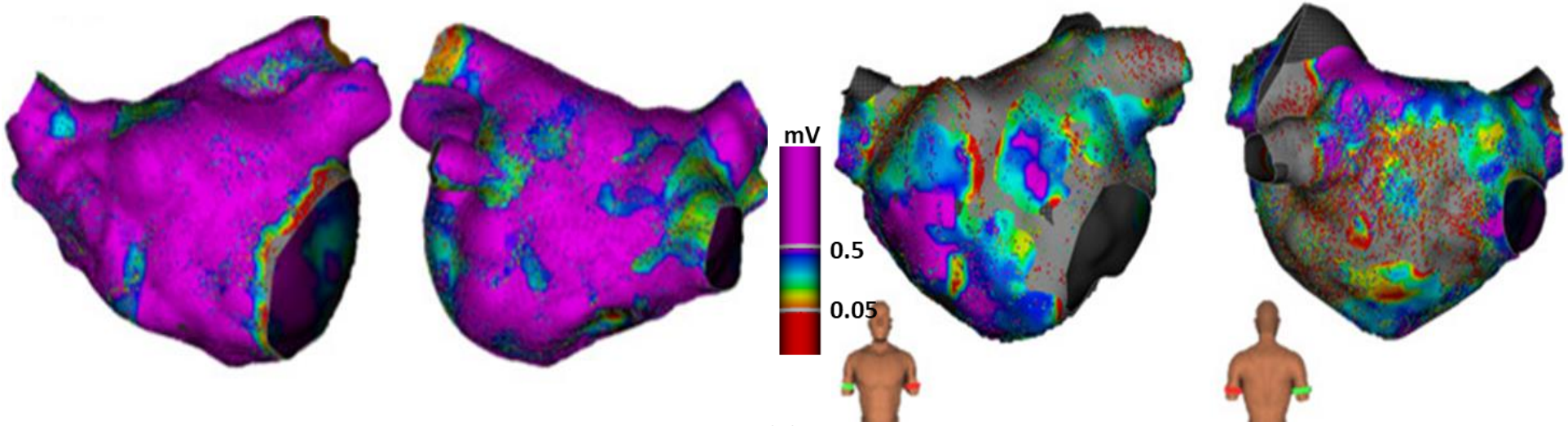


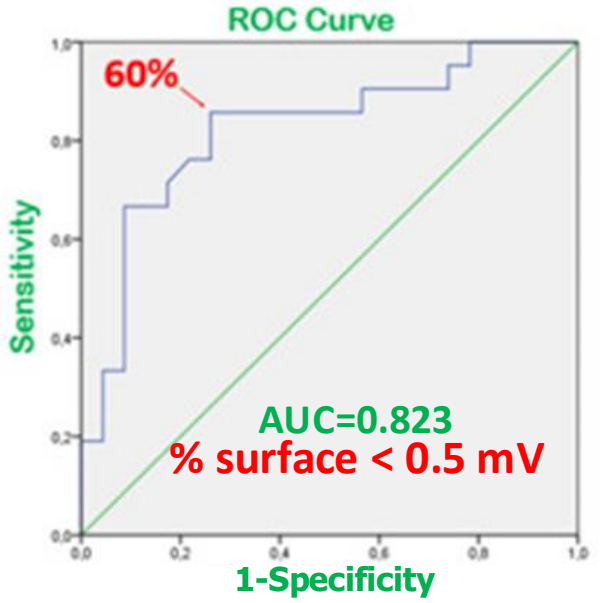
PV outlet area (posterior wall/ LA dome/ “box region”) : predominant initial location

Goette A et al, Europace 2024;26(9):euae204.

- *Caixal G et al, Europace 2021;23:1559–67.*
- *Hopman L et al, Eur Heart J Cardiovasc Imaging 2022;23:1182–90.*

Electroanatomical mapping: low-voltage extent predicts recurrence





Laraichi Z, Lațcu DG et al, Arch Cardiovasc Dis Suppl 2023;15(1):98

WAVE-MAP AF

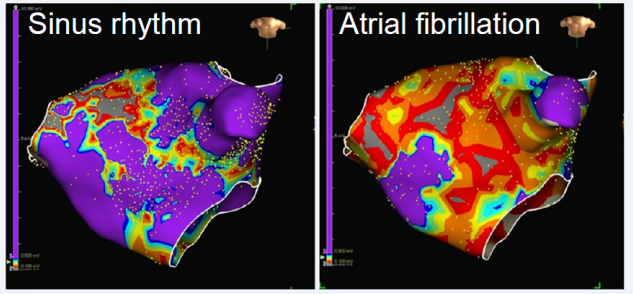
QUESTION **Is low voltage substrate, as identified by advisor HD grid HD wave solution configuration, associated with 12-month recurrence rates after a single pulmonary vein isolation procedure?**

POPULATION

300 subjects
113 Paroxysmal AF
86 Early persistent AF
101 Non-early persistent AF

18 centers
Europe and Israel

MAPPING



Baseline sinus rhythm and atrial fibrillation maps collected
Off-line calculation of low voltage area (*n* = 196)

INTERVENTION

PVI only ablation in all subjects

FINDING

Starek Z et al, Europace (2023) 25, 1–11

75.5%

free from arrhythmia recurrence at 12 months

Larger low voltage area, *not AF diagnosis,* **associated with increased risk of arrhythmia recurrence after single PVI:**

Sinus rhythm

>28% of the left atrium below 0.5 mV
(HR: 4.82, 95% CI: 2.08–11.18, *P* = 0.0003)

Atrial fibrillation:

>72% of the left atrium below 0.5 mV
(HR: 5.66, 95% CI: 2.34–13.69, *P* = 0.0001)

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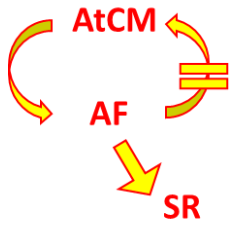
8. **SR maintains SR**

- after 24 hours of SR: vulnerability to AF decreased (43%), whereas after 1 week of SR the inducibility of AF was comparable to control (29%).
- Six hours after conversion to SR the median duration of electrically induced paroxysms of AF was already back to normal and lasted only 7±2 seconds.
- AF interval was significantly prolonged from 105±10 to 139±7 ms.
- After 1 week of SR the rate adaptation of the atrial refractory period was fully normalized and also at slow heart rates the refractory period was normal again.

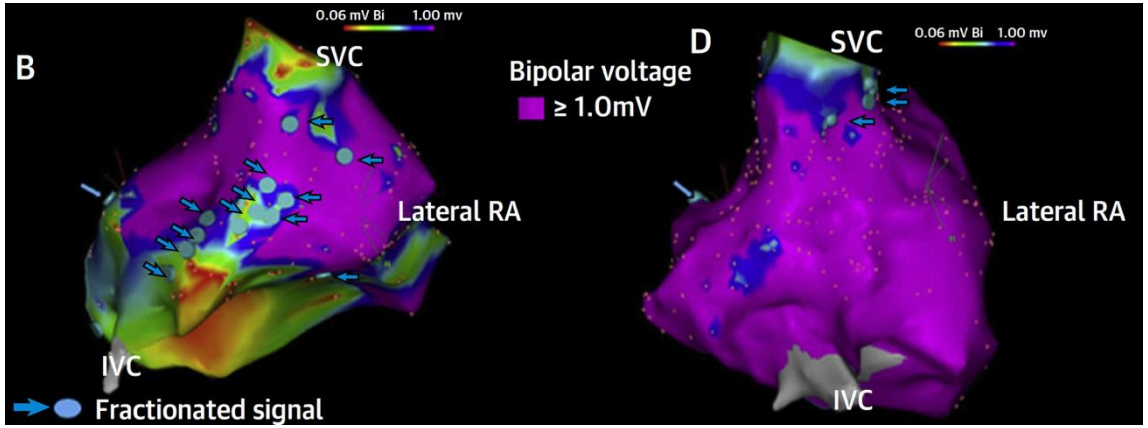
"after cardioversion of AF, all electrophysiological changes induced by atrial fibrillation are completely reversible within a few days"

M C Wijffels, C J Kirchhof, R Dorland, M A Allessie, Circulation 1995 Oct 1;92(7):1954-68.



Long-Term Follow-Up of CAMERA-MRI Study

- Patients with >90% reduction in AF burden
- Time to FU RA mapping after initial ablation was 23.4 ±11.9 months



	Baseline	Follow-Up	Change	p Value
Bipolar voltage				
Global, mV	1.58 ± 0.1	1.87 ± 0.1	+0.29 ± 0.1	0.04
Low voltage				
Global, %	19.7 ± 3.0	14.2 ± 3.2	−5.5 ± 2.9	0.07
Fractionation				
Global, %	21.7 ± 3.5	8.3 ± 1.8	−13.4 ± 3.6	0.002

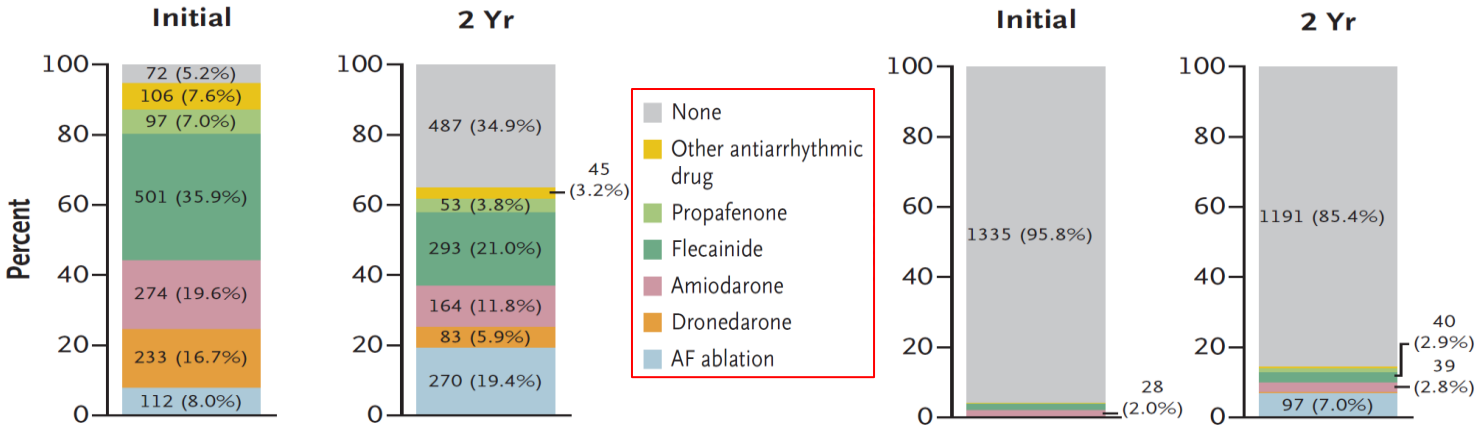
Sugumar H et al, JACC Clin Electrophysiol 2019;5:681–8

Kirchhof P et al, N Engl J Med. 2020 Oct 1;383(14):1305-1316

EAST – AFNET 4 trial population
2789 patients with atrial fibrillation diagnosed within a year prior to randomization and cardiovascular conditions approximating a CHA_2DS_2VASc score of ≥ 2
2633 with known AF-related symptoms (EHRA score) at baseline
randomized to Early Rhythm Control or Usual Care

Early Rhythm Control in all patients (n=1305/2633)	**Usual Care, including symptom-directed rhythm control therapy** (n=1328/2633)

CV death, stroke, or hospitalization for HF or ACS

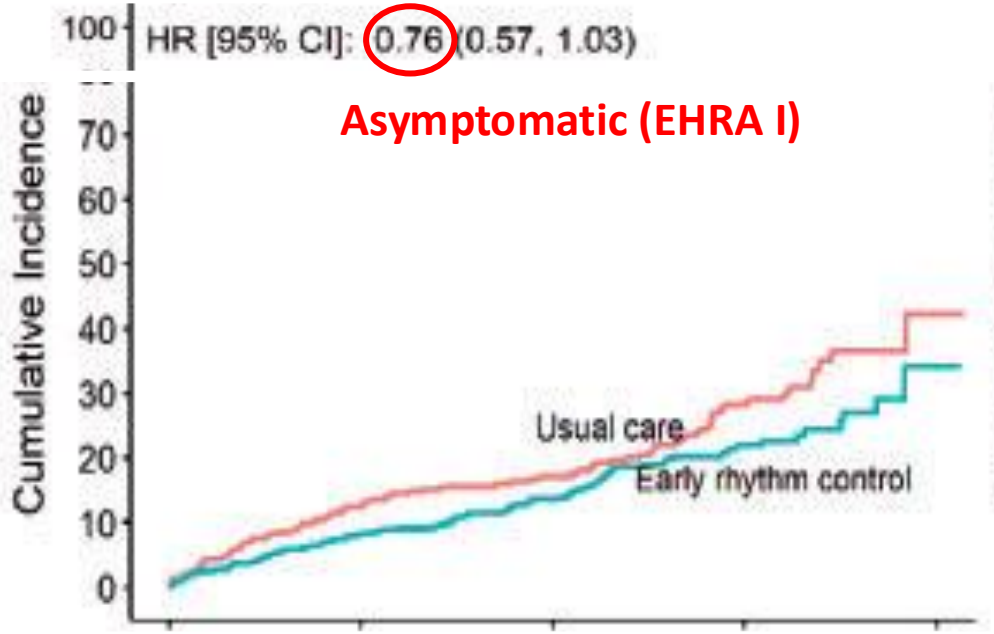


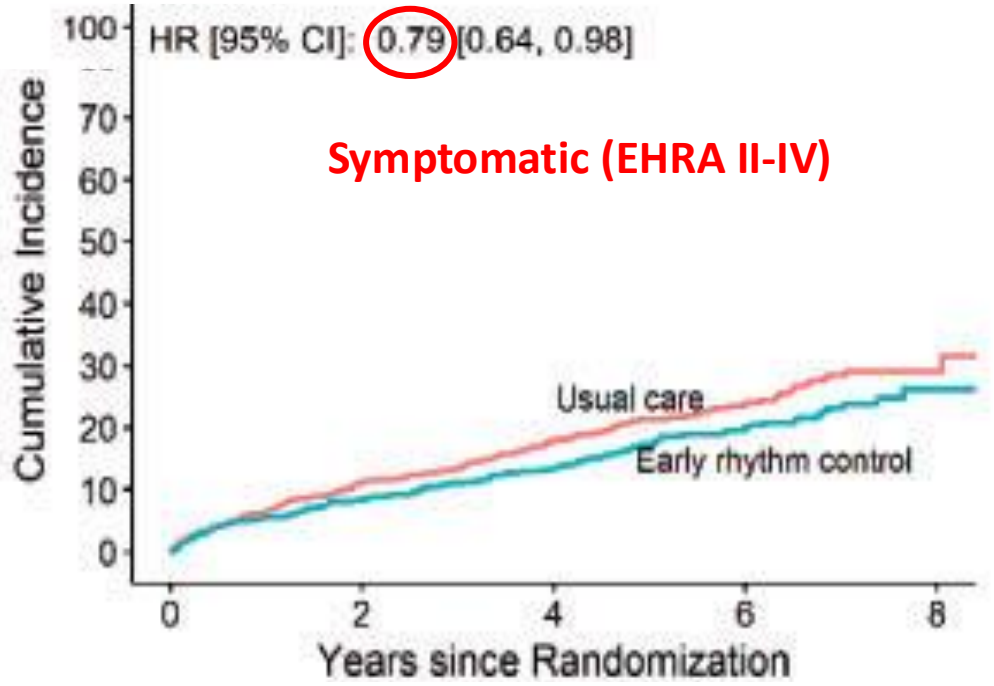
Asymptomatic at baseline (n=395)	**Symptomatic** at baseline (n=910)	**Asymptomatic** at baseline (n=406)	**Symptomatic** at baseline (n=922)

No difference in treatment pattern between asymptomatic and symptomatic patients.
Excellent symptom control in both randomized groups at two years.

Ca. 1/4 treated with AF ablation and 3/4 treated with antiarrhythmic drugs at 2 years

Ca. 8% treated with AF ablation and 9% treated with antiarrhythmic drugs at 2 years

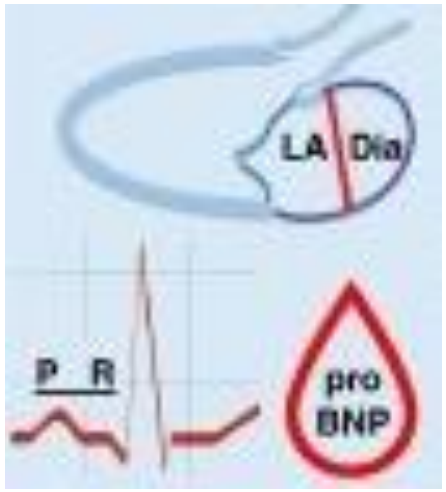




*Willem S et al, European Heart Journal (2022) **43**, 1219–1230*

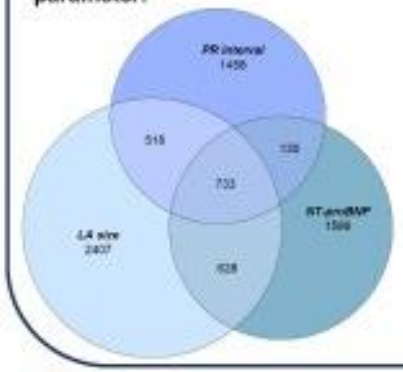
Early Rhythm Control in patients with and without atrial cardiomyopathy

EAST-AFNET 4



EAST-AFNET 4: 2810 pts with early AF

Data availability of parameter:



Classification of atrial cardiomyopathy:

1. None:
- all in lower tertile

2. Mild:
- all combinations in lower/middle tertile

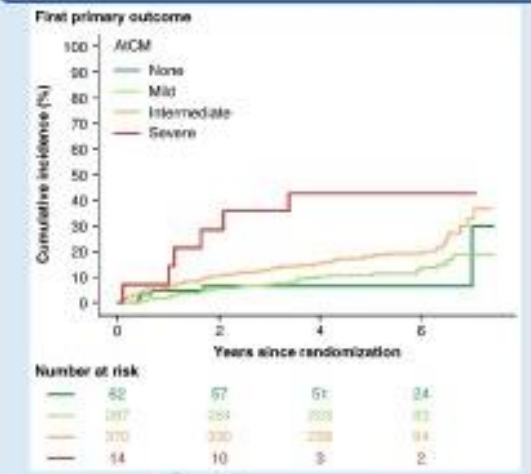
3. Intermediate:
- 1–2 in upper tertile

4. Severe:
- all in upper tertile

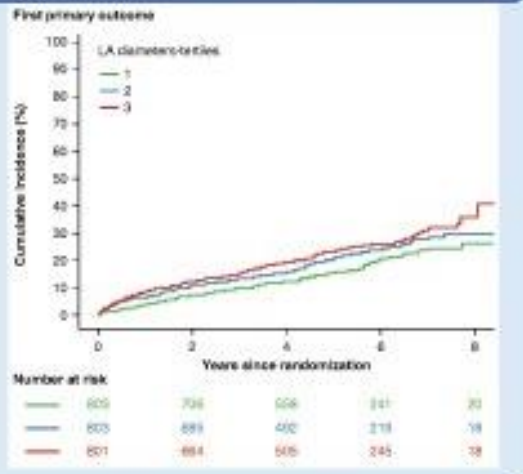
Baseline characteristics of atrial cardiomyopathy parameter:

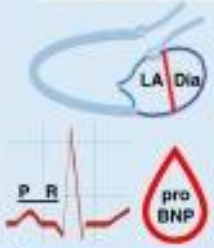
- 69% with enlarged left atria (>41 mm ♂ ; >39 mm ♀)
- 23% with prolonged PR interval (>200 ms)
- 56% with increased NT-proBNPlevels (>365 pg/ml)

Stratified by AtCM severity



Stratified by LA size





Increasing LA size was associated with more primary outcome and higher risk of recurrent AF

AtCM severity was associated with more primary outcome and higher risk of recurrent AF

Early rhythm-control therapy is effective and safe with and without atrial cardiomyopathy.

Primary outcome

CV death, stroke, or hospitalization for HF or ACS

	Early rhythm control				Usual care			
	None	Mild	Intermediate	Severe	None	Mild	Intermediate	Severe
events/person-yr (incidence/100 person-yr)	4/182 (2.2)	19/756 (2.5)	28/810 (3.5)	0/21 (0)	1/136 (0.7)	16/614 (2.6)	46/875 (5.3)	6/27 (22.4)

Goette A et al, Europace 2025 Oct 7;27(10):euaf256.