

17° Meeting



CardioLucca
Heart Brings Heart **2023**

Lucca, 22-24 Giugno 2023
Centro Congressi Auditorium San Francesco

Management terapeutico personalizzato della fibrillazione atriale di recente insorgenza

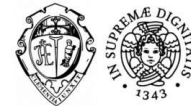
Giulio Zucchelli

MD, PhD, FESC

Direttore f.f.

UO Cardiologia 2 – Azienda Ospedaliero Universitaria Pisana

mail: g.zucchelli@ao-pisa.toscana.it



Caso Clinico

Maschio, 44 anni

Professione: Venditore di macchine

Pratica nuoto a livello amatoriale

Novembre 2016: singolo episodio di palpitazione dopo esercizio fisico



Caso Clinico



ECG

Ritmo sinusale. FC 63 bpm. PR e QTc normale

Ecocardiogramma

Normale EF (63%), Atrio sinistro non dilatato (volume 30 ml/mq)

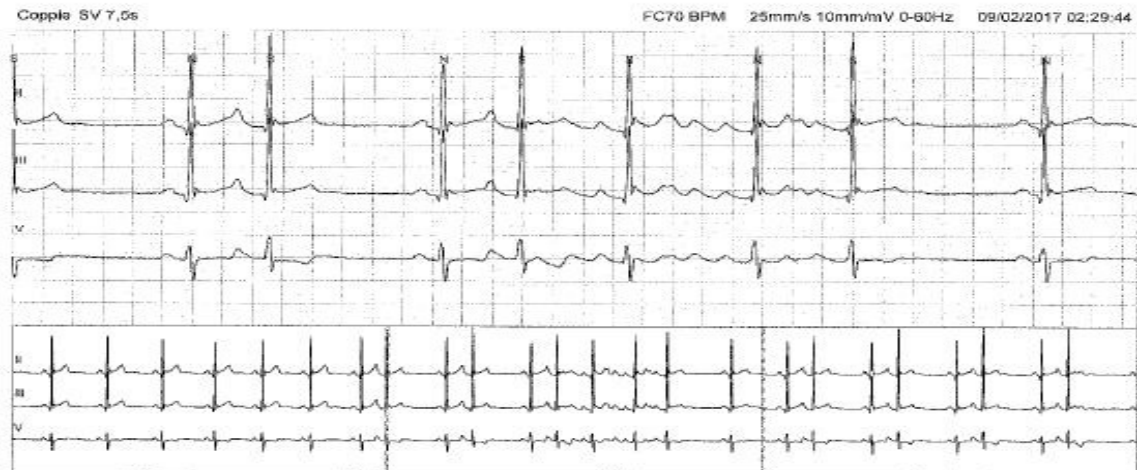
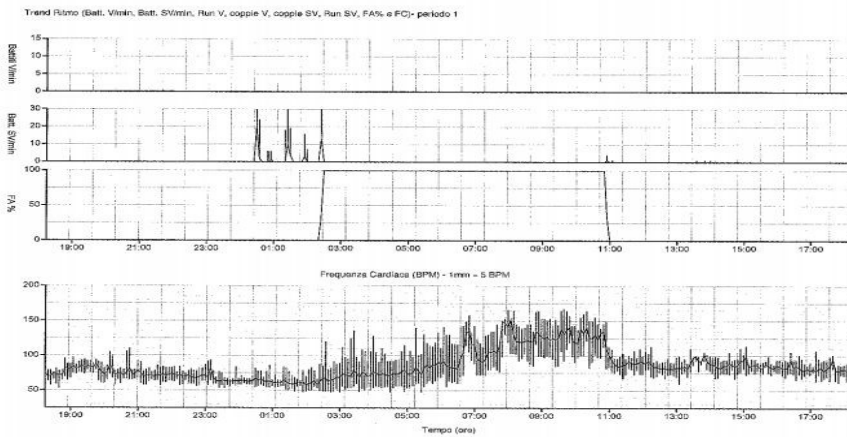
Holter ECG

- FAP
- P on T

Durante aritmia

Non chiari sintomi

Trend



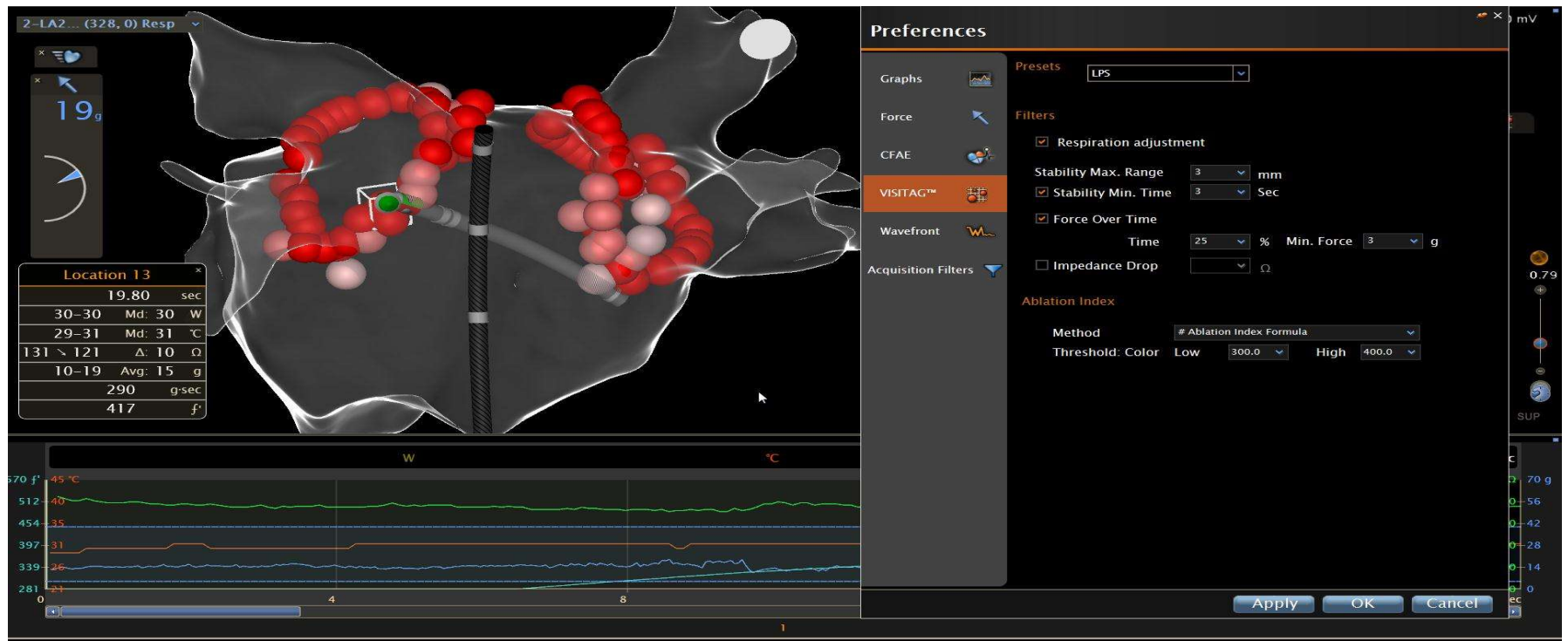
Terapia



Bisoprolol 2.5 mg/die-----nessun effetto su Holter ECG

Flecainide 100 mg x2/die----nessun effetto su Holter ECG

CHADS-VASC=0 > no AC




FEBBRAIO 2017

ISOLAMENTO VENE POLMONARI CON RADIOFREQUENZA

Follow-up

- Nessun evento a 5 anni (ECG, ECG Holter, TTM)

RISULTATI (Tutto)			
FREQUENZA CARDIACA : (Totale QRS : 106645) (Durata Ora : 22:40)			
Media : 78 bpm	FC Max : 110 bpm a (1)16:23:28	RR Max : 1100 ms a (1)07:13:34	
Giorno (08:00 - 21:00) : 85 bpm	FC Min : 54 bpm a (1)07:13:34	RR Min : 540 ms a (1)18:34:39	
Notte (23:00 - 06:00) : 69 bpm			
BRADICARDIA : 0	PAUSE : 0	BATTITI MANCATI : 0	
EPISODI VENTRICOLARI :			
BATTITI ECTOP. :	BI & TRIGEMIN. : 0 & 0	TACHICARDIA : 0	
Isolati : 0	0.0 %		
Coppie : 0	0.0 %		
Salve : 0	0.0 %		
Totale : 0			
EPISODI SOPRAVENTRICOLARI :			
BATTITI ECTOP. :	BI & TRIGEMIN. : 0 & 0	TACHICARDIA : 0	INSTABILITA' RR : 0
Isolati : 15	0.0 %		
Coppie : 0	0.0 %		
Salve : 0	0.0 %		
Totale : 15			
COMMENTI			
Ritmo sinusale mediamente normofrequente (FC media 77 bpm, FC max 110 bpm, FC min 54 bpm). PR e QT nei limiti. Extrasistolia sopraventricolare isolata a rarissima incidenza . Non pause significative. Non sintomi in diario.			
			
PARAMETRI D'ANALISI : Data Registrazione : 05/09/2018 a 16:12 Durata : 23:59:54 REGISTRATORE N° : S8005083 310C			
Picco Minimo :	2500ms	Intervallo < :	450ms
Presenza di Sopraventricolare < :	75%	Tachicardia Sopraventricolare > :	1000ms
Presenza di Ventricolare < :	OFF	Tachicardia Ventricolare > :	500ms



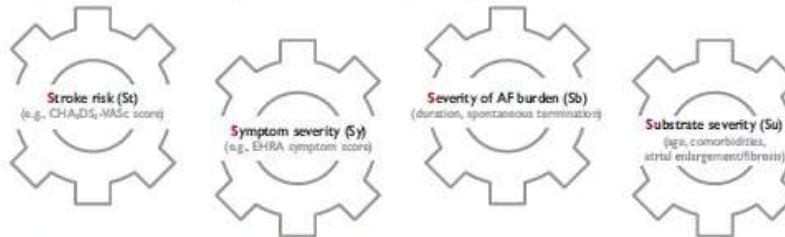
CC To ABC

Confirm AF

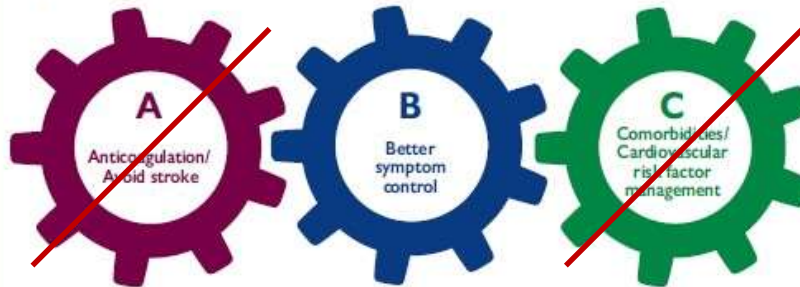


A 12-lead ECG or a rhythm strip showing AF pattern for ≥ 30 s

Characterise AF (the 4S-AF scheme)



Treat AF: The ABC pathway



1. Identify low-risk patients
CHA₂DS₂-VASc 0(m), 1(f)
2. Offer stroke prevention if
CHA₂DS₂-VASc ≥ 1 (m), 2(f)
Assess bleeding risk, address
modifiable bleeding risk factors
3. Choose OAC (NOAC or VKA
with well-managed TTR)

- Assess symptoms,
QoL and patient's
preferences
- Optimize rate
control
- Consider a rhythm
control strategy
(CV, AADs, ablation)

- Comorbidities and
cardiovascular risk
factors
- Lifestyle changes
(obesity reduction,
regular exercise,
reduction of alcohol use,
etc.)

©ESC 2020

CHADS-VASC=0

Comorbidità/substrato= 0

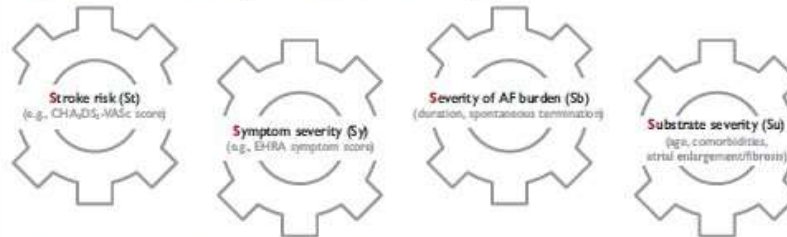
CC To ABC

Confirm AF

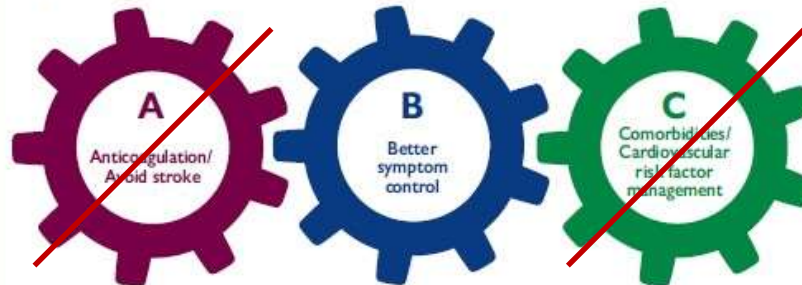


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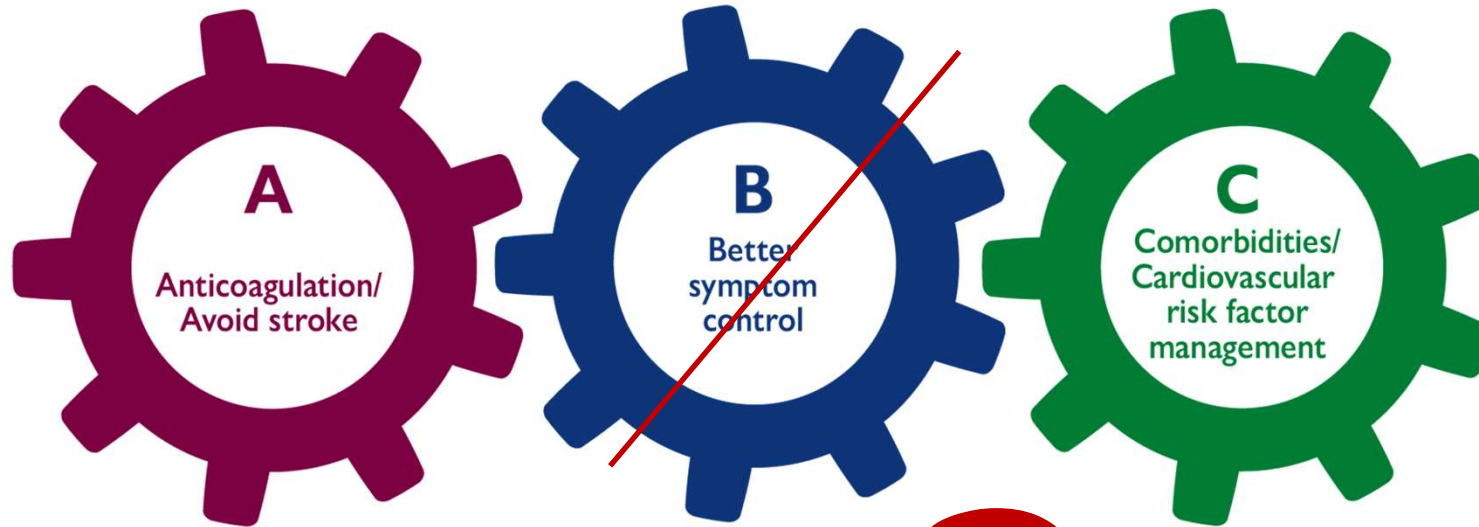
CHADS-VASC=0

Comorbidità/substrato= 0

EHRA=1

Burden AF 20%

Treat AF: The ABC pathway



1. Identify low-risk patients
CHA₂DS₂-VASc 0(m), 1(f)
2. Offer stroke prevention if
CHA₂DS₂-VASc ≥1(m), 2(f)
Assess bleeding risk, address
modifiable bleeding risk factors
3. Choose OAC (NOAC or VKA
with well-managed TTR)

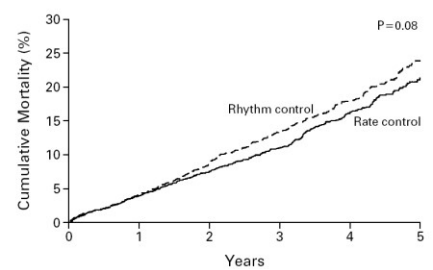
Assess symptoms,
QoL and patient's
preferences

Optimize rate
control

Consider a rhythm
control strategy
(CV, AADs, ablation)

Comorbidities and
cardiovascular risk
factors

Lifestyle changes
(obesity reduction,
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reduction of alcohol use,
etc.)



The New England Journal of Medicine
 Copyright © 2002 by the Massachusetts Medical Society
 VOLUME 347 DECEMBER 5, 2002 NUMBER 23

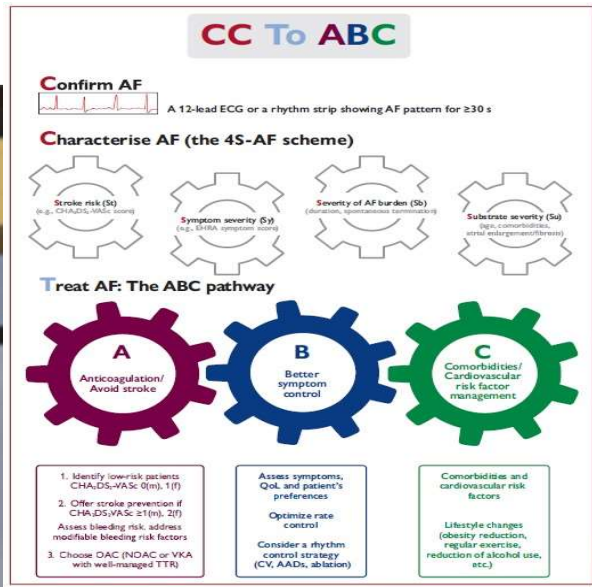
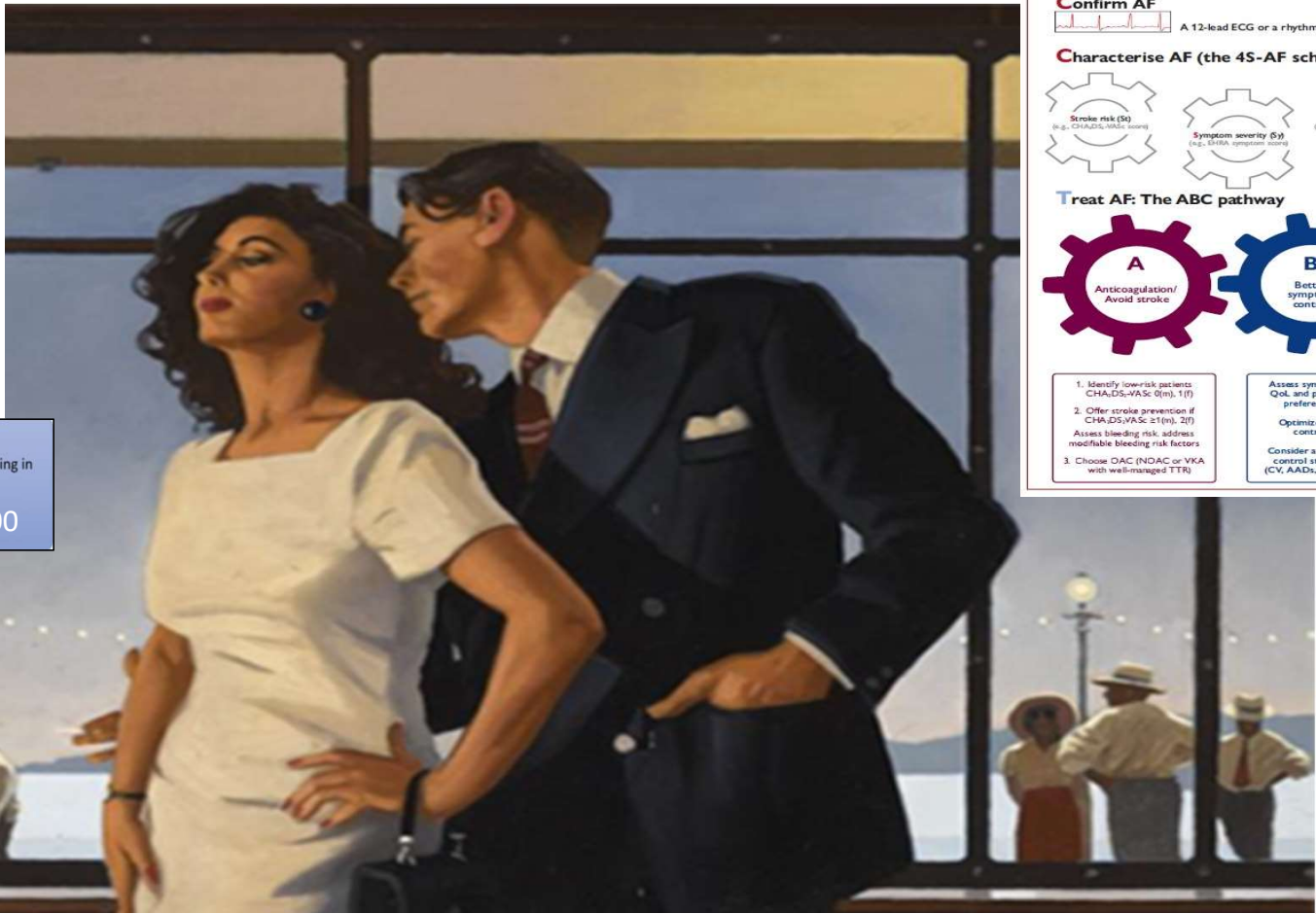
A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

THE ATRIAL FIBRILLATION FOLLOW-UP INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) INVESTIGATORS*

Cardiovert & Forget

After Cardioversion, refrain from OAC resulting in increased prevalence of thromboembolic complications

2000



L'amore è fatto anche di equivoci, di cui ci si accorge solo quando finisce

The New England Journal of Medicine

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VOLUME 347

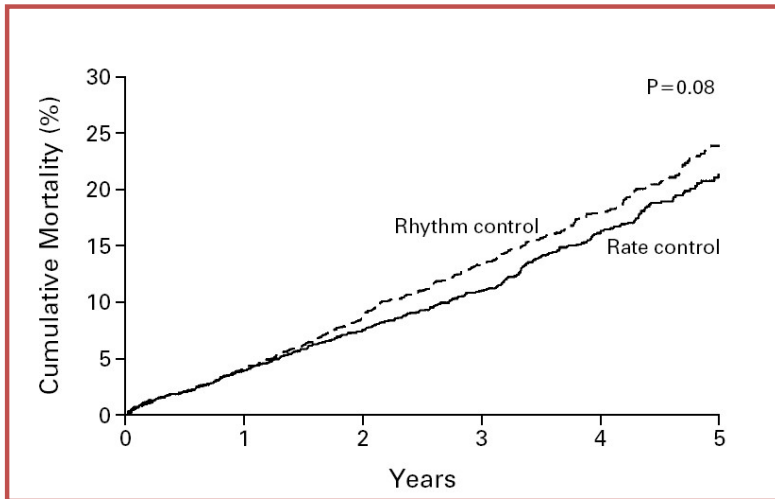
DECEMBER 5, 2002

NUMBER 23

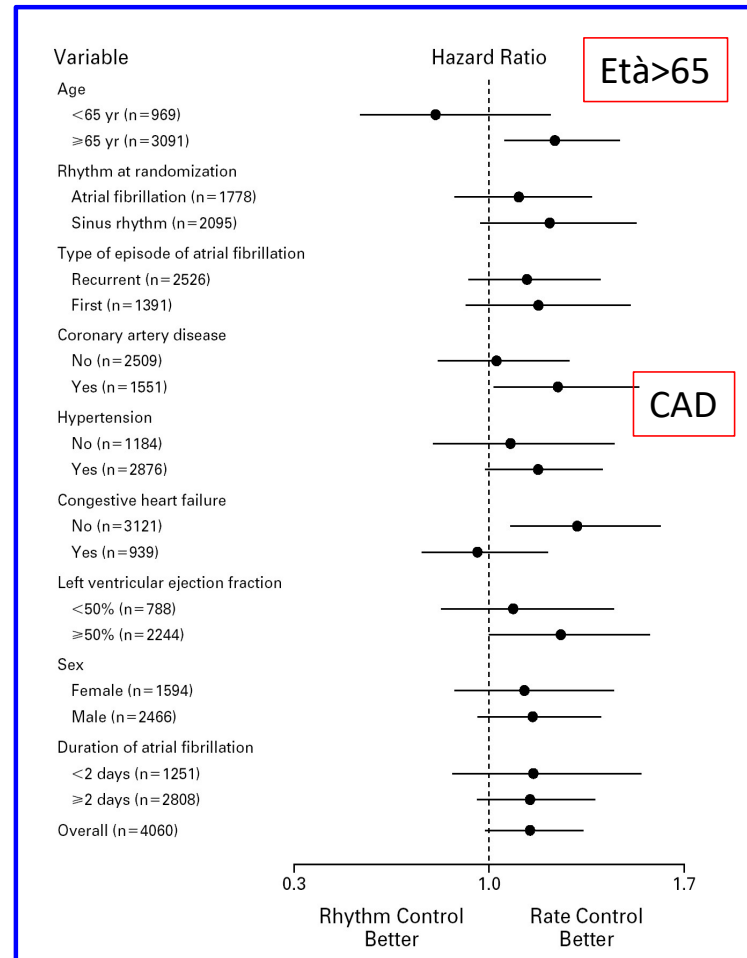


A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

THE ATRIAL FIBRILLATION FOLLOW-UP INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) INVESTIGATORS*



LANDMARK



Rate vs rhythm control

2002-2020 a long journey

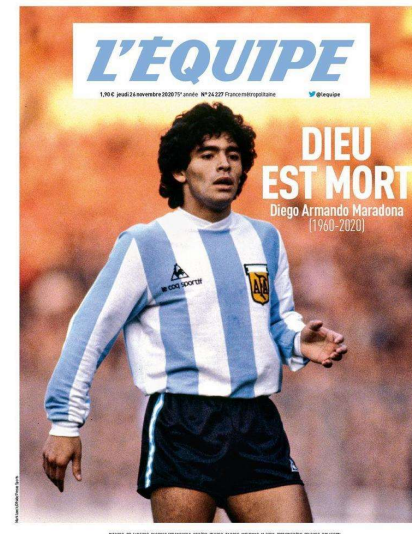
2002: AFFIRM/RACE

Euro begins its official circulation in 12 European countries

The change affected over 300 million Europeans

A circular graphic with a white border containing text and an image of Euro banknotes and coins. The background of the circle is a gradient from green at the top to purple at the bottom.

2020: EAST_AFNET4 trial



The EAST—AFNET 4 combined several of the concepts that were developed after the disappointing results of the earlier rate vs. rhythm trials. These include:

- enrollment of patients with early AF, diagnosed less than a year prior to enrolment,
- mandated continuation of anticoagulation and treatment of the cardiovascular conditions throughout the trial in all patients,
- providing guidance on the safe use and delivery of rhythm control therapy, and
- using both antiarrhythmic drugs, AF ablation, and their combination to achieve rhythm control.

The **NEW ENGLAND**
JOURNAL of MEDICINE

ESTABLISHED IN 1812

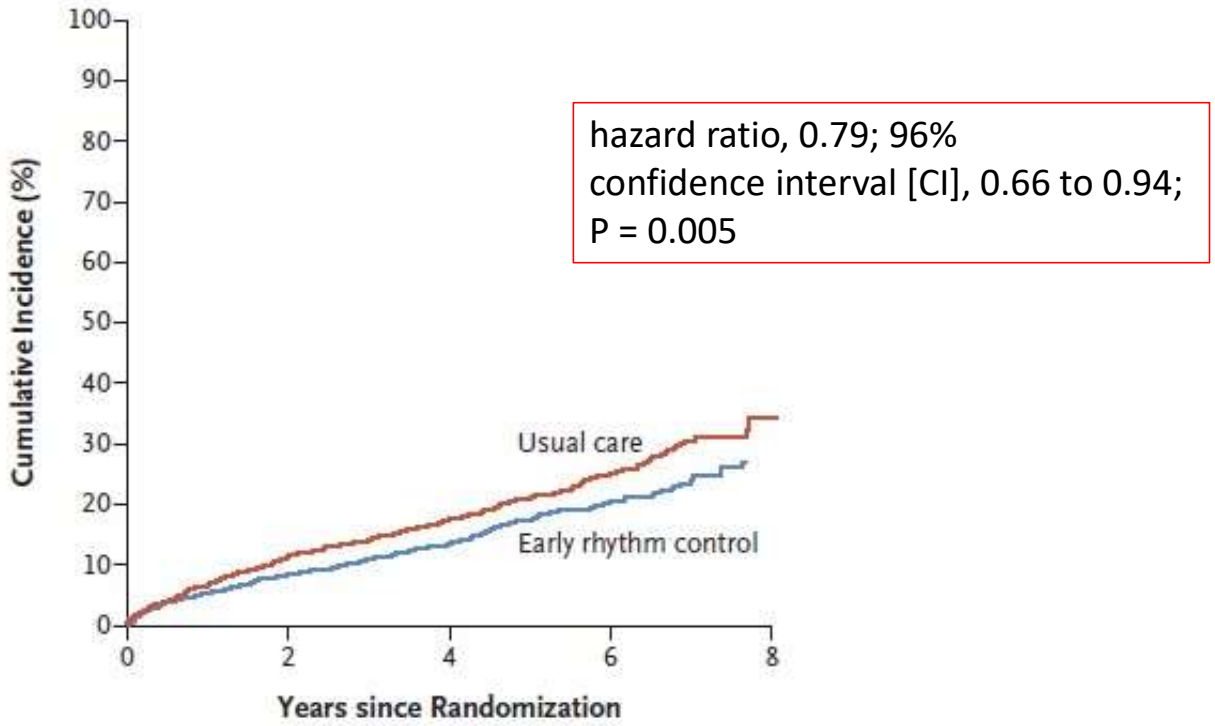
OCTOBER 1, 2020

VOL. 383 NO. 14

Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

P. Kirchhof, A.J. Camm, A. Goette, A. Brandes, L. Eckardt, A. Elvan, T. Fetsch, I.C. van Gelder, D. Haase, L.M. Haegeli, F. Hamann, H. Heidbüchel, G. Hindricks, J. Kautzner, K.-H. Kuck, L. Mont, G.A. Ng, J. Rekosz, N. Schoen, U. Schotten, A. Suling, J. Taggeselle, S. Themistoclakis, E. Vettorazzi, P. Vardas, K. Wegscheider, S. Willems, H.J.G.M. Crijns, and G. Breithardt, for the EAST-AFNET 4 Trial Investigators*

The first primary outcome was:
death from CV causes, stroke, or
hospitalization with worsening of heart failure or acute coronary syndrome



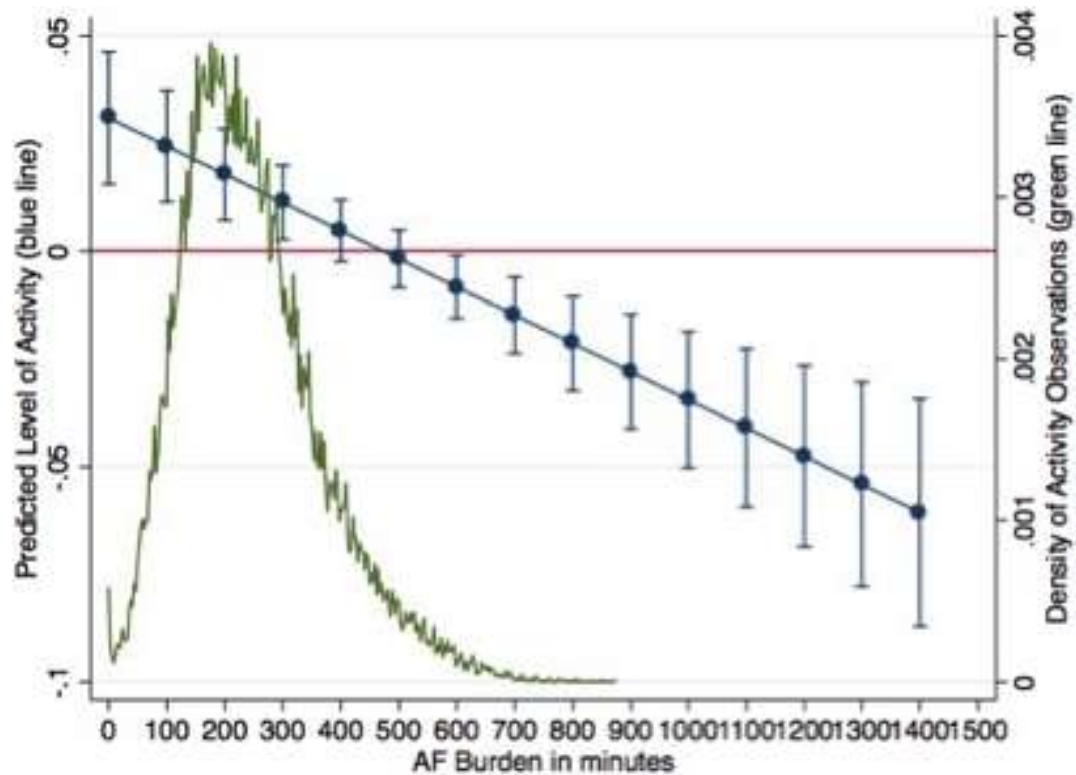
No. at Risk	0	2	4	6	8
Usual care	1394	1169	888	405	34
Early rhythm control	1395	1193	913	404	26

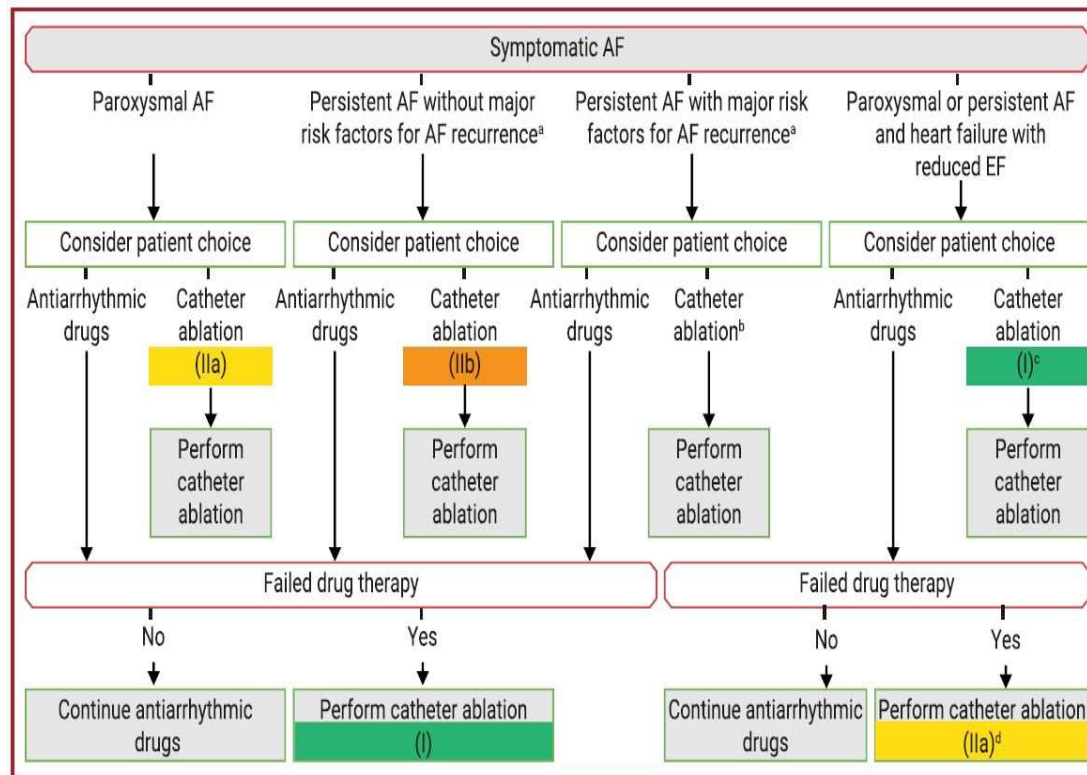
Characteristic	Early Rhythm Control (N = 1395)	Usual Care (N = 1394)
Age — yr	70.2±8.4	70.4±8.2
Female sex — no. (%)	645 (46.2)	648 (46.5)
Body-mass index†	29.2±5.4	29.3±5.4
Type of atrial fibrillation — no./total no. (%)		
First episode	528/1391 (38.0)	520/1394 (37.3)
Paroxysmal	501/1391 (36.0)	493/1394 (35.4)
Persistent	362/1391 (26.0)	381/1394 (27.3)
Sinus rhythm at baseline — no./total no. (%)	762/1389 (54.9)	743/1393 (53.3)
Median days since atrial fibrillation diagnosis (IQR)‡	36.0 (6.0–114.0)	36.0 (6.0–112.0)
Absence of atrial fibrillation symptoms — no./total no. (%)§	395/1305 (30.3)	406/1328 (30.6)
Previous cardioversion — no./total no. (%)	546/1364 (40.0)	543/1389 (39.1)
Concomitant cardiovascular conditions		
Previous stroke or transient ischemic attack — no. (%)	175 (12.5)	153 (11.0)
At least mild cognitive impairment — no./total no. (%)¶	582/1326 (43.9)	584/1341 (43.5)
Arterial hypertension — no. (%)	1230 (88.2)	1220 (87.5)
Blood pressure — mm Hg		
Systolic	136.5±19.4	137.5±19.3
Diastolic	80.9±12.1	81.3±12.0
Stable heart failure — no. (%)**	396 (28.4)	402 (28.8)
CHA ₂ DS ₂ -VASc score††	3.4±1.3	3.3±1.3
Valvular heart disease — no./total no. (%)	609/1389 (43.8)	642/1391 (46.2)
Chronic kidney disease of MDRD stage 3 or 4 — no. (%)‡‡	172 (12.3)	179 (12.8)
Medication at discharge — no./total no. (%)§§		
Oral anticoagulation with NOAC or VKA	1267/1389 (91.2)	1250/1393 (89.7)
Digoxin or digitoxin	46/1389 (3.3)	85/1393 (6.1)
Beta-blocker	1058/1389 (76.2)	1191/1393 (85.5)
ACE inhibitors or angiotensin II receptor blocker	953/1389 (68.6)	979/1393 (70.3)
Mineralocorticoid-receptor antagonist	90/1389 (6.5)	92/1393 (6.6)
Diuretic	559/1389 (40.2)	561/1393 (40.3)
Statin	628/1389 (45.2)	568/1393 (40.8)
Platelet inhibitor	229/1389 (16.5)	226/1393 (16.2)

No symptoms in 30%



Correlation between atrial fibrillation burden and patient activity level: insights from the DISCERN AF Study

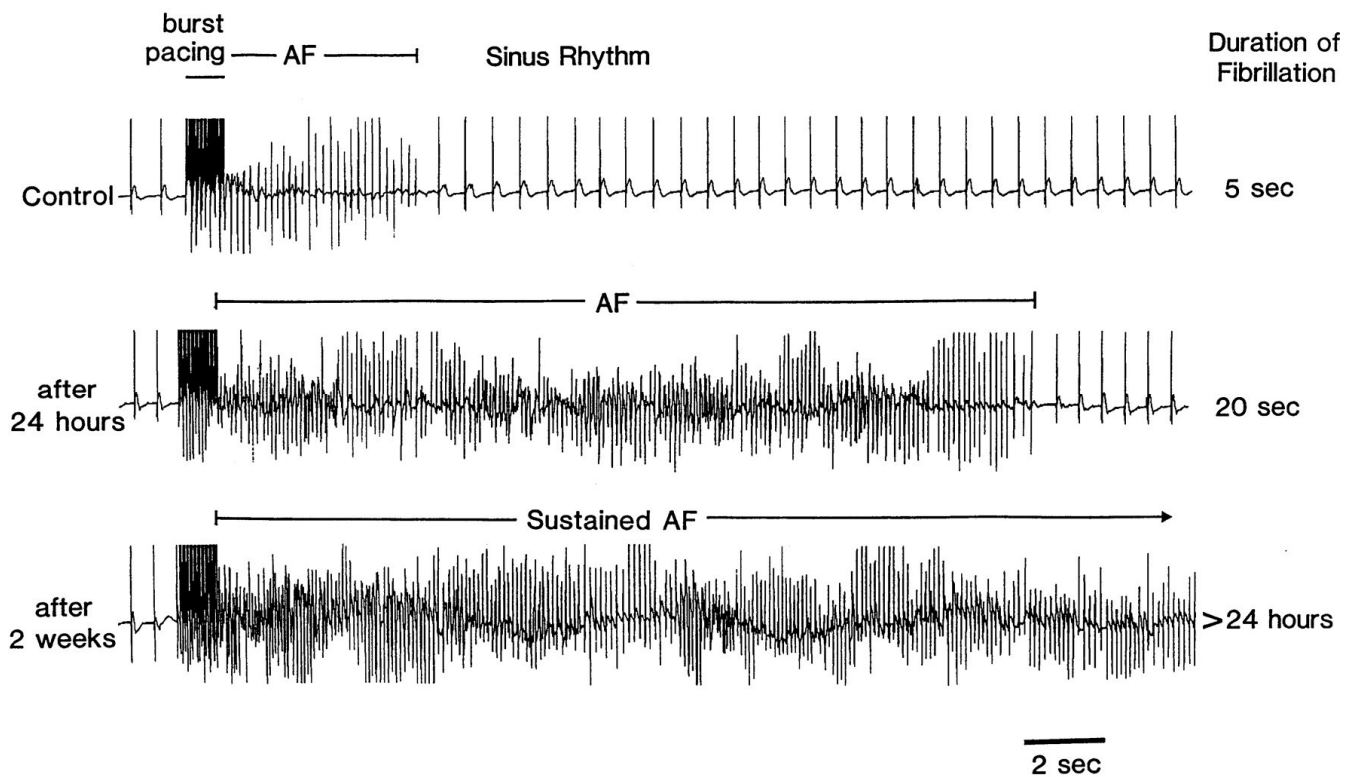




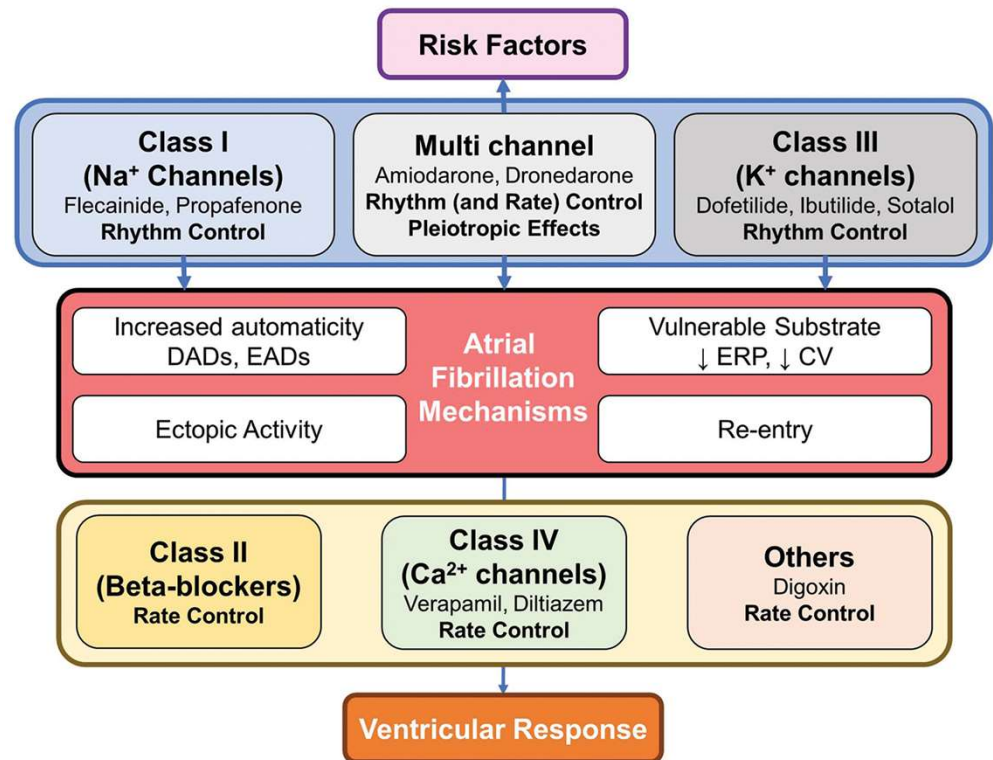
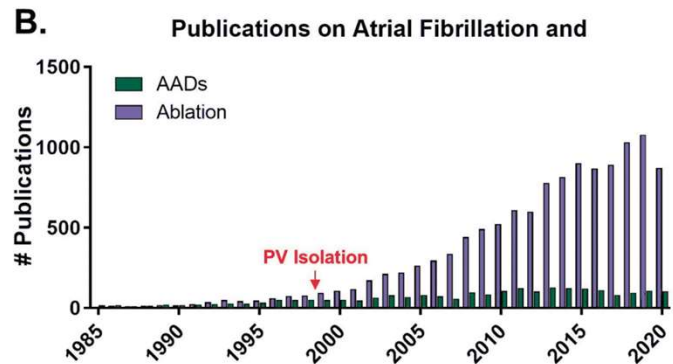
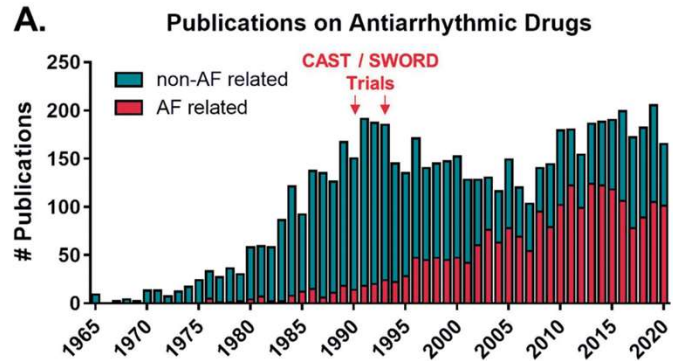
→ Discussione con paziente nella scelta della terapia

Qual è il ruolo dei farmaci antiaritmici?

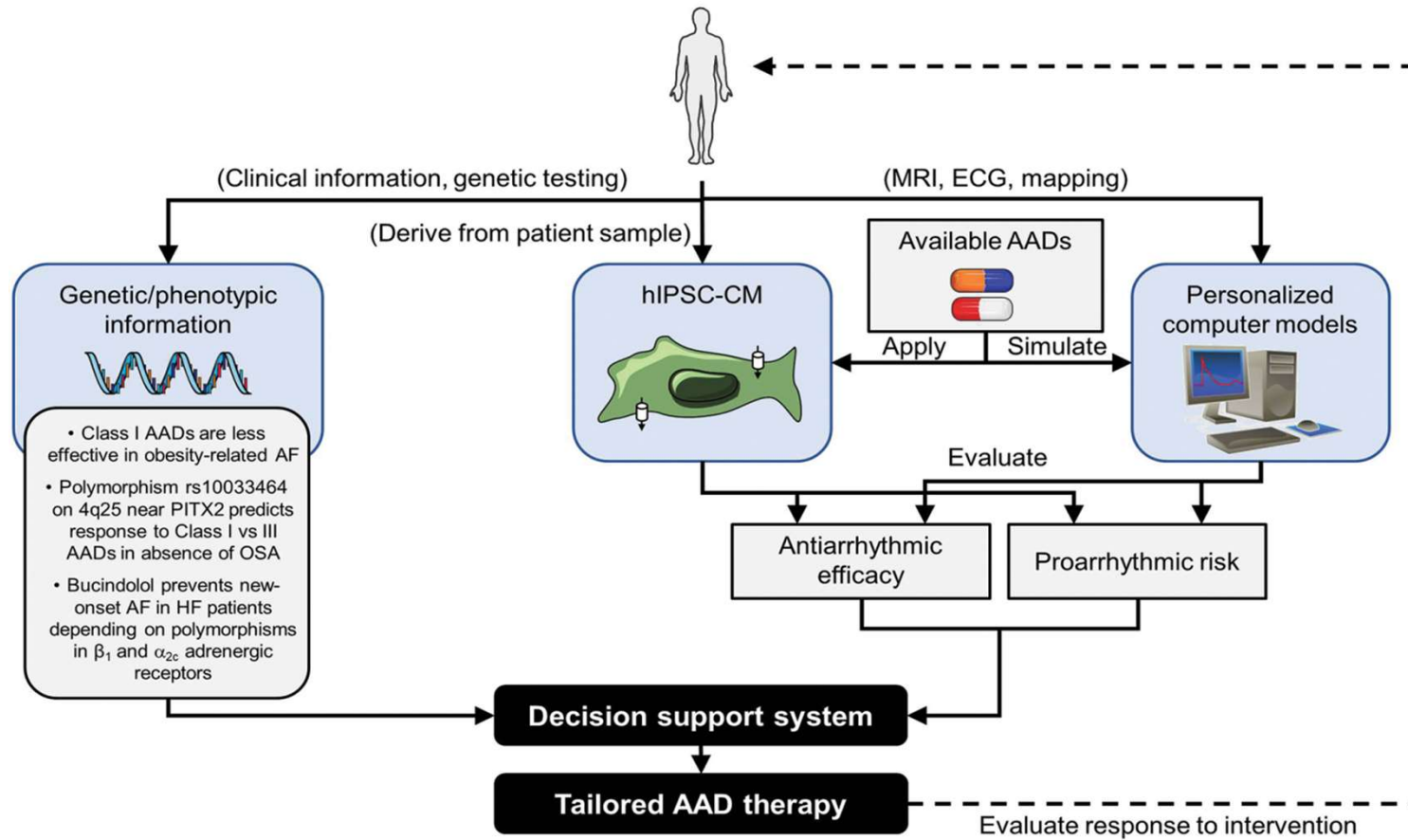
“Friends if taken with moderation”



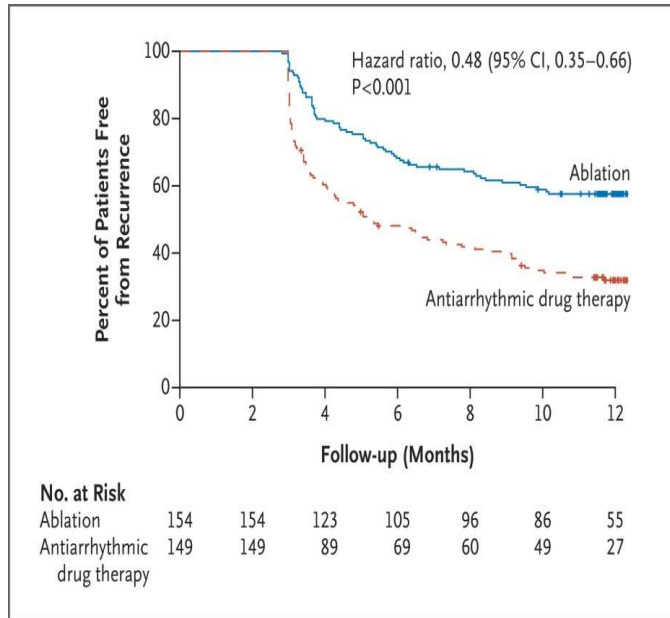
*Wijffels, Allesie MA. Atrial fibrillation begets atrial fibrillation. A study in awake chronically instrumented goats. *Circulation* 1995 ;92:1954–6



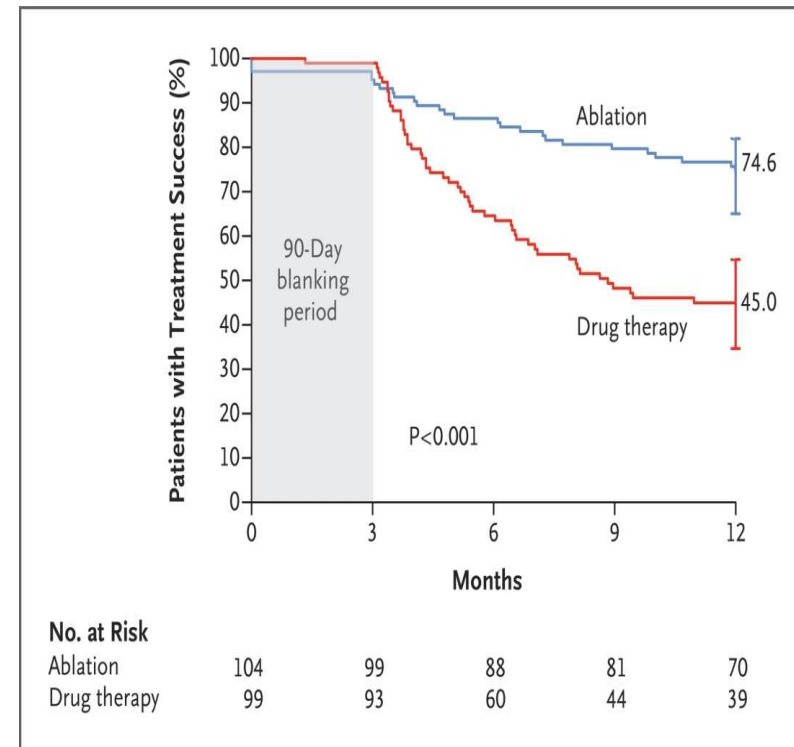
Precision Medicine and AADs



Cryo first line



EARLY-AF trial–NEJM 2020



STOP-AF first –NEJM 2020

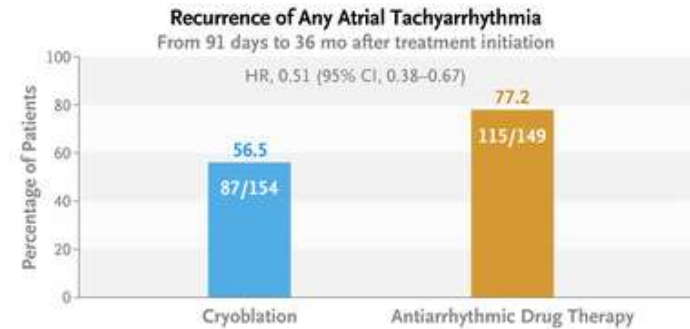
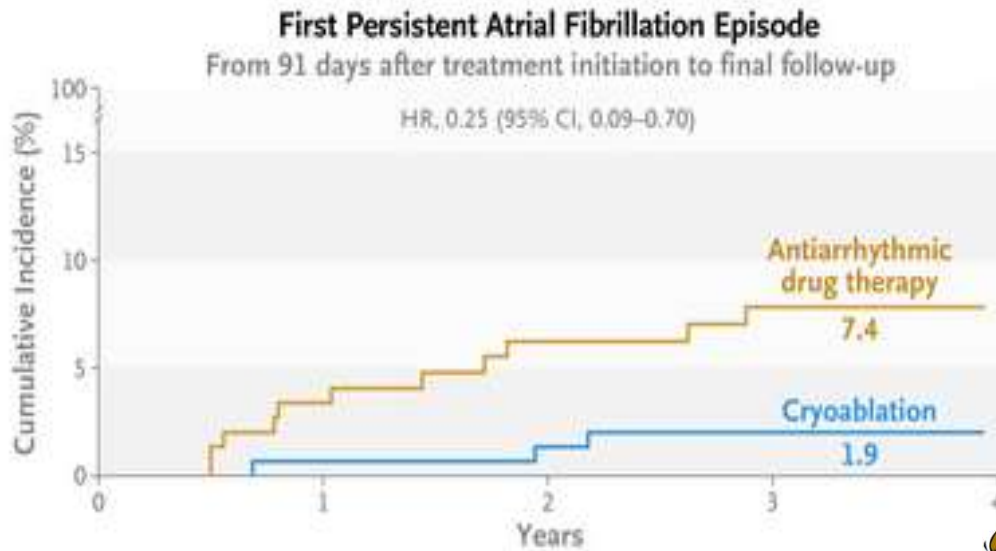
Guarda il burden!



RESEARCH SUMMARY

Progression of Atrial Fibrillation after Cryoablation or Drug Therapy

Andrade JG et al. DOI: 10.1056/NEJMoa2212540



End point ablation

Techniques and technologies		
Complete electrical isolation of the pulmonary veins is recommended during all AF catheter-ablation procedures. ^{235–237,239,606,608–610,613,614,678,679,681,683,684,686,713,731,759,780}	I	A
If patient has history of CTI-dependent AFL or if typical AFL is induced at the time of AF ablation, delivery of a CTI lesion may be considered. ^{731–733,819–821}	IIb	B
Use of additional ablation lesions beyond PVI (low voltage areas, lines, fragmented activity, ectopic foci, rotors, and others) may be considered but is not well established. ^{677,680,708,711–730}	IIb	B

Consensus 2012 Afib abl

Isolamento delle vene polmonari (PVI) con check almeno del *blocco in entrata* è "la pietra angolare" della procedura.

Monitoring 20'

TABLE 3: RECOMMENDATIONS REGARDING ABLATION TECHNIQUE

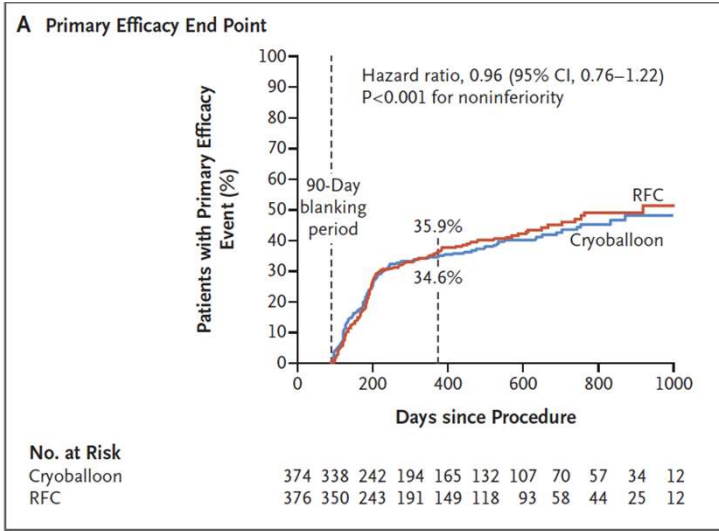
- Ablation strategies that target the PVs and/or PV antrum are the cornerstone for most AF ablation procedures.
- If the PVs are targeted, electrical isolation should be the goal.
- Achievement of electrical isolation requires, at a minimum, assessment and demonstration of entrance block into the PV.
- Monitoring for PV recrudescence for 20 minutes following initial PV isolation should be considered.
- For targeted PV isolation, entrance and/or exit block should be demonstrated.
- Careful identification of the PV antra is mandatory to avoid ablation within the PVs.

Callens, HRS/EHRA/ECAS consensus. Europace 2012, March 1

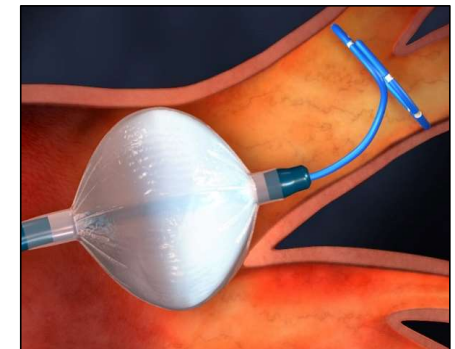
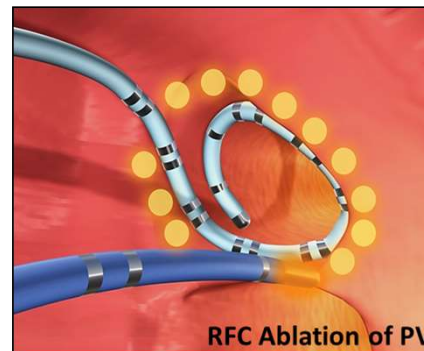
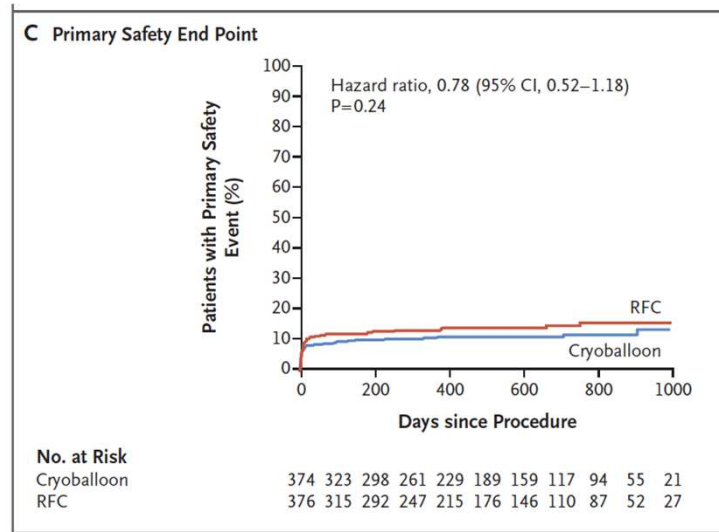
Complete electrical isolation of PVs

Eur Heart J, 2020,
<https://doi.org/10.1093/eurheartj/ehaa612>

FIRE & ICE Trial



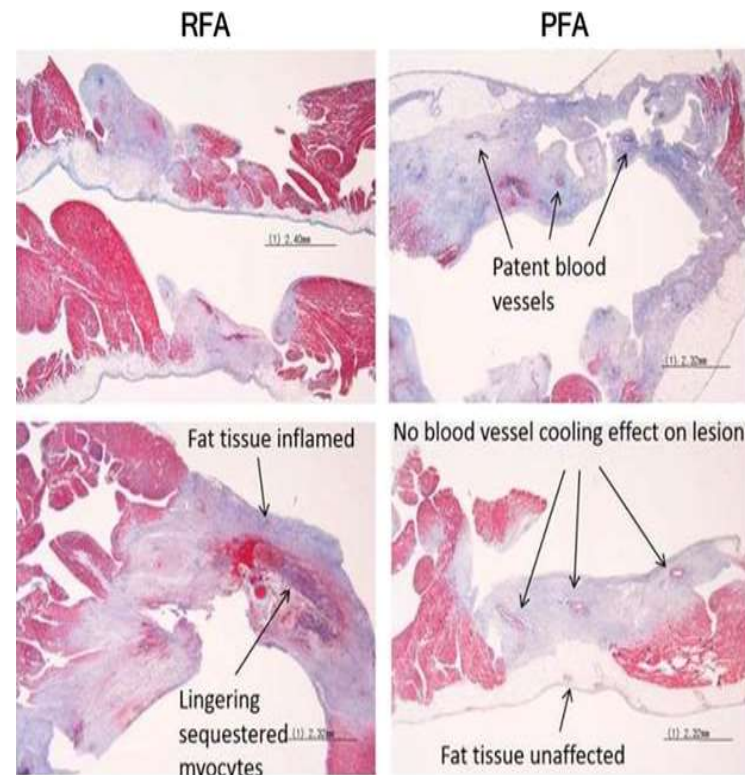
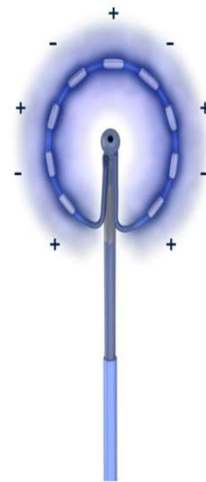
Time Measurement (minutes)	RFC (n=376)	Cryoballoon (n=374)	p-value **
Procedure Time ***	140.9 ± 54.9	124.4 ± 39.0	<0.0001
LA Dwell Time ***	108.6 ± 44.9	92.3 ± 31.4	<0.0001
Fluoroscopy Time	16.6 ± 17.8	21.7 ± 13.9	<0.0001



Kuck KH, et al. *N Engl J Med.* 2016; 374(23): 2235-45.

Pulsed Field Ablation vs RF/thermal Energy

- Extremely fast
- Deep, coherent lesions
- No/little heat
- Tissue-selective





Fibrillazione atriale persistente:
La terra di mezzo

The logo for the ATHENA study, featuring the word "ATHENA" in large, white, serif capital letters stacked vertically. The background is a dark, fiery scene with a silhouette of a person running or jumping.

P.I. Giulio Zucchelli

Promotore Azienda Ospedaliero Universitaria Pisana

Study Design

Study Type ⓘ : Observational

Estimated Enrollment ⓘ : 4100 participants

Observational Model: Cohort

Time Perspective: Prospective

Official Title: Advanced TecHnologies For SuccEssful AblatioN of AF in Clinical Practice: ATHENA Study

Actual Study Start Date ⓘ : January 1, 2022

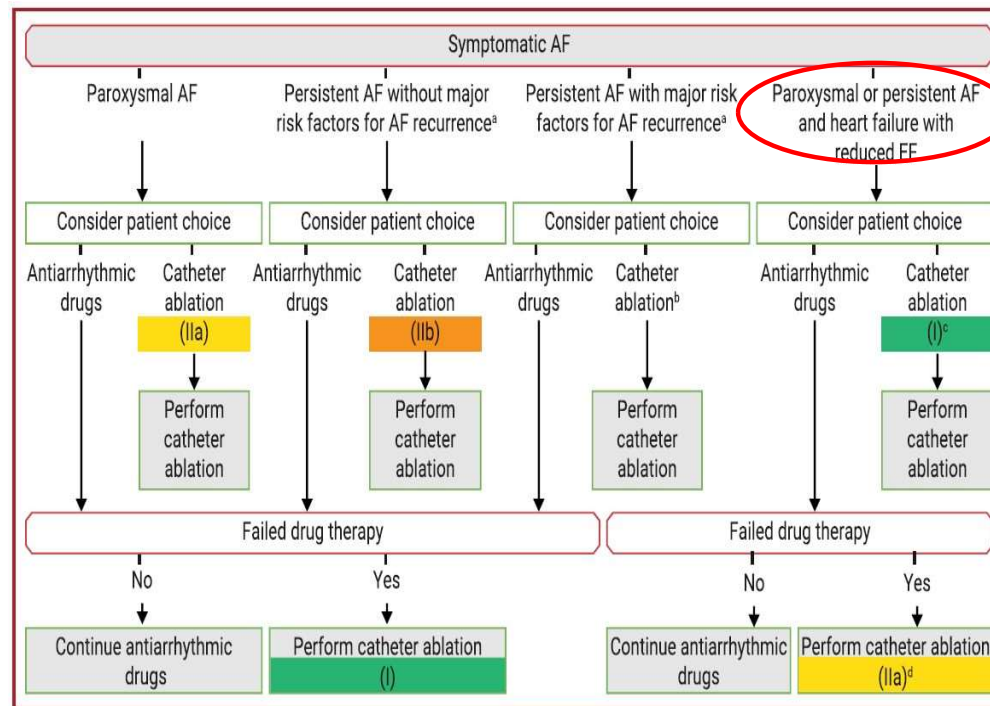
Estimated Primary Completion Date ⓘ : December 2027

Estimated Study Completion Date ⓘ : January 2029

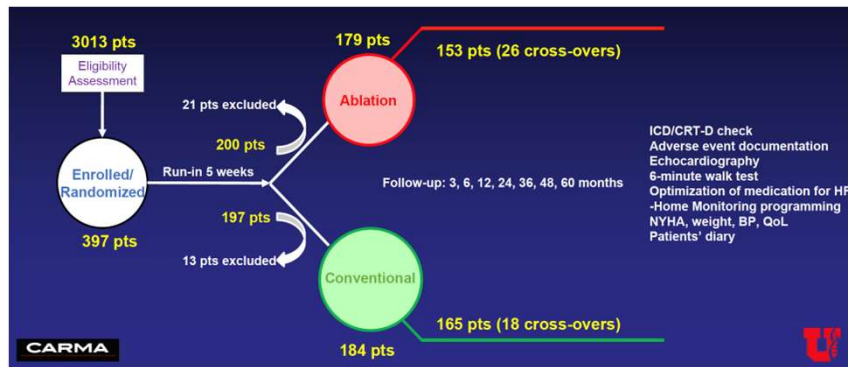
The primary objective

Clinical and **Procedural** parameters predicting the recurrence-free at the medium-long term follow-up

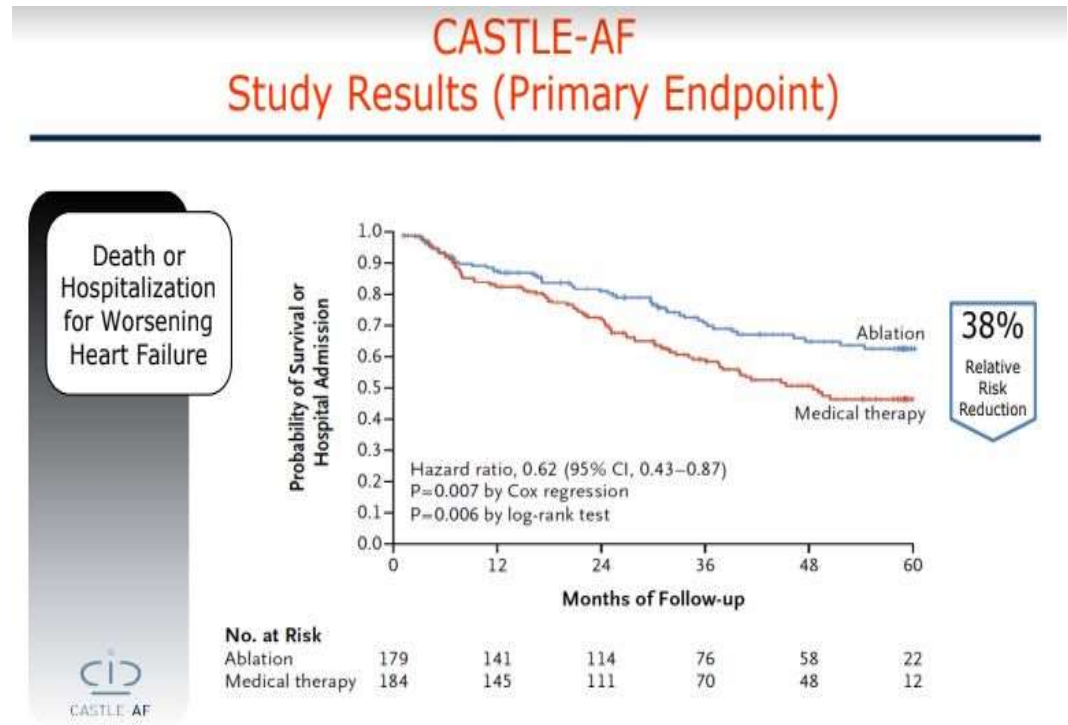
Afib Heart Failure patients



CASTLE - AF

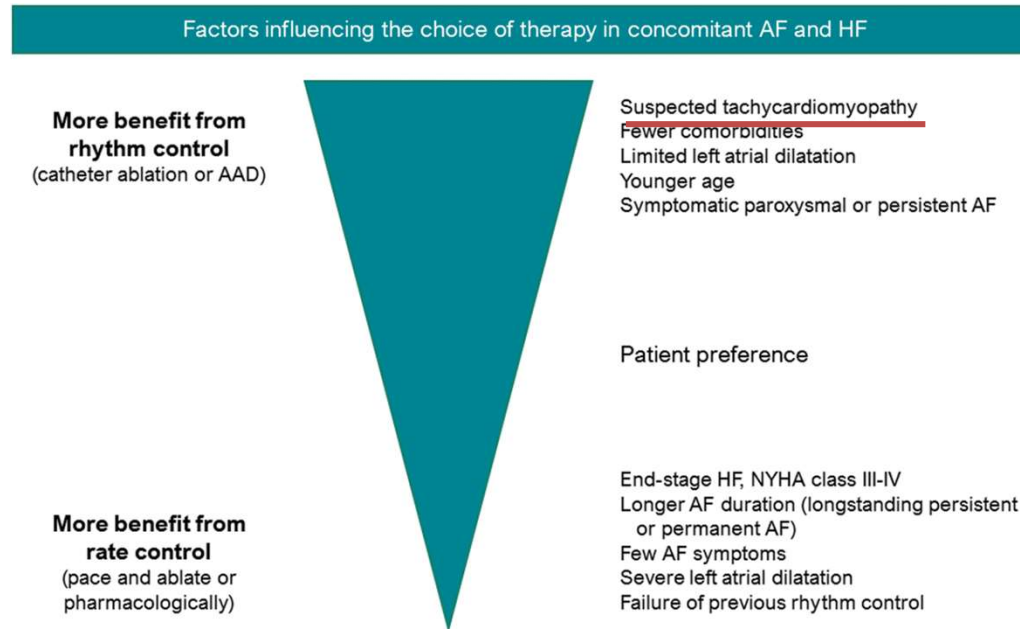


Total number of enrollees: 363
 duration of follow-up: median 37.8 months
 mean patient age: 64 years
 mean left ventricular ejection fraction: 35%
AF long standing: 25%

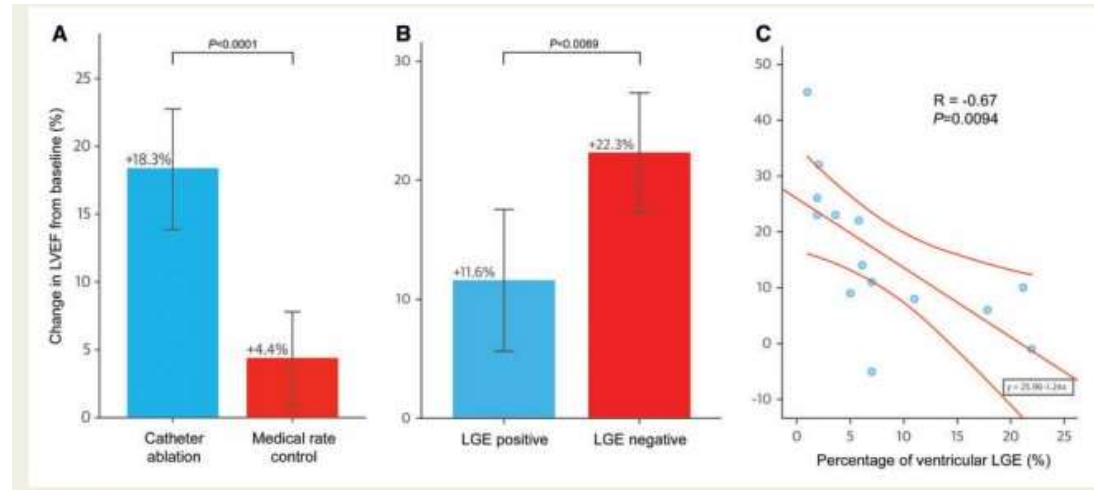


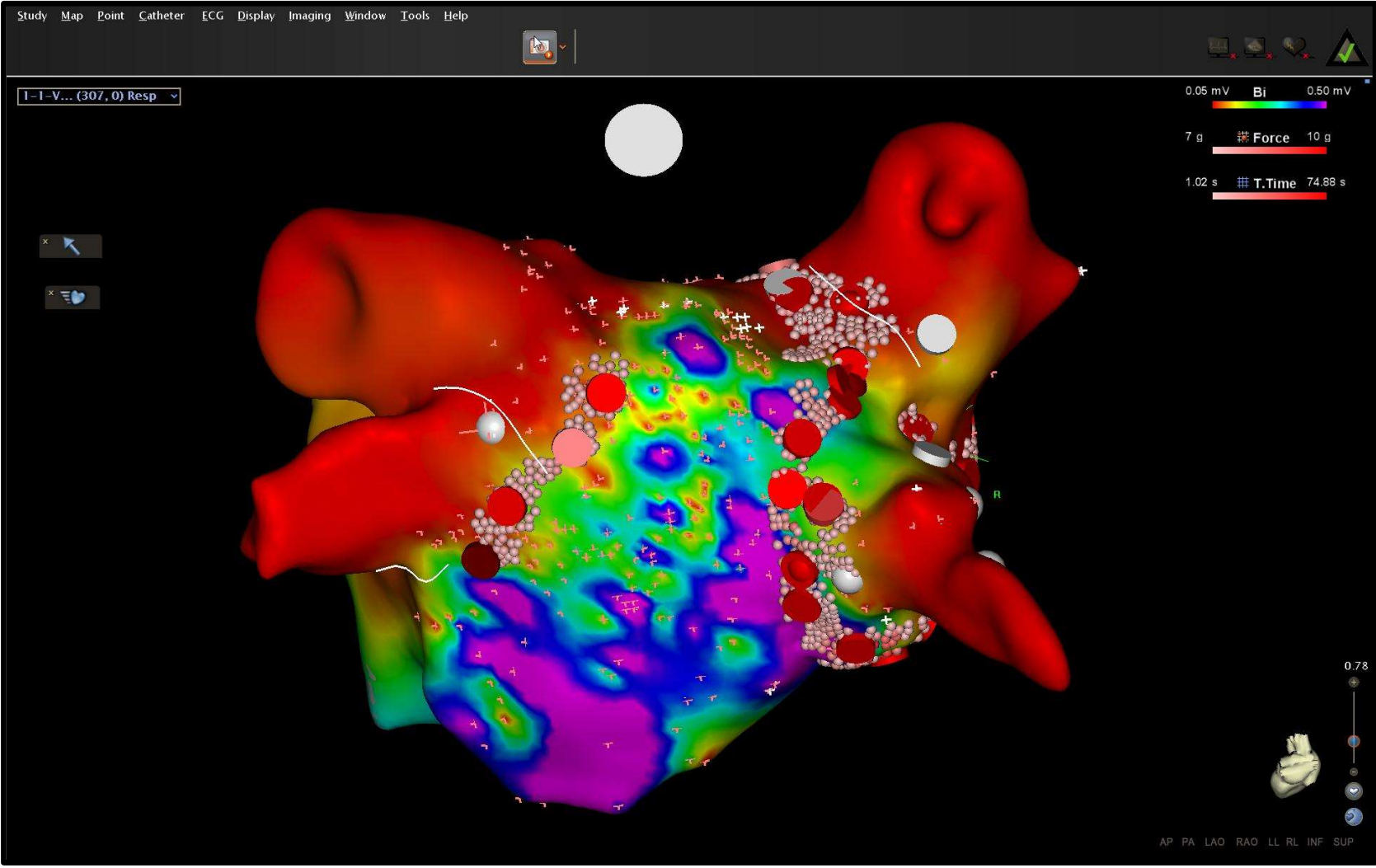
Marrouche NF and Brachmann J, et al.; NEJM 2018; 378:417-427

Personalization in HF pts with AFib

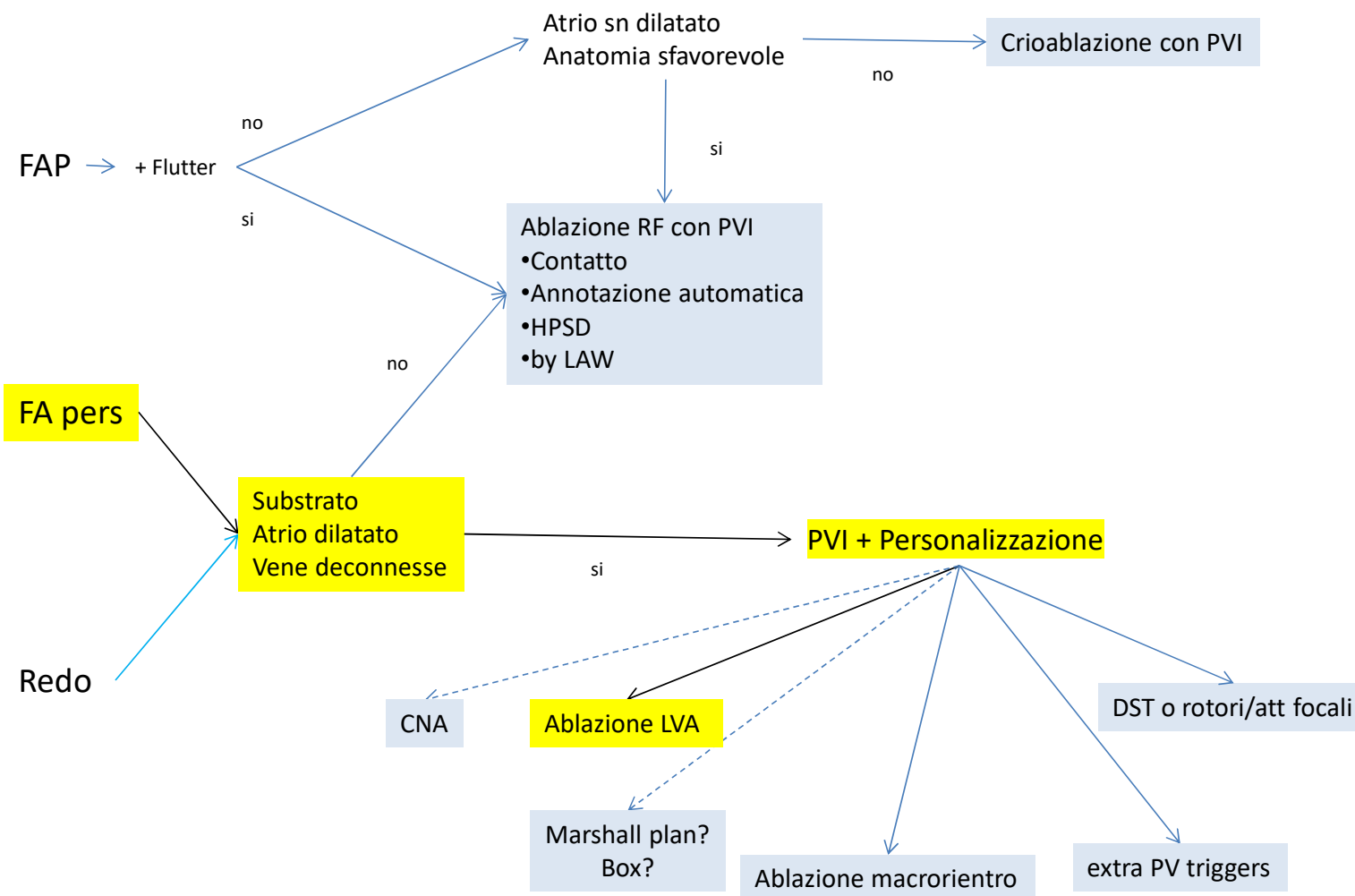


Ventricular LGE for candidates?



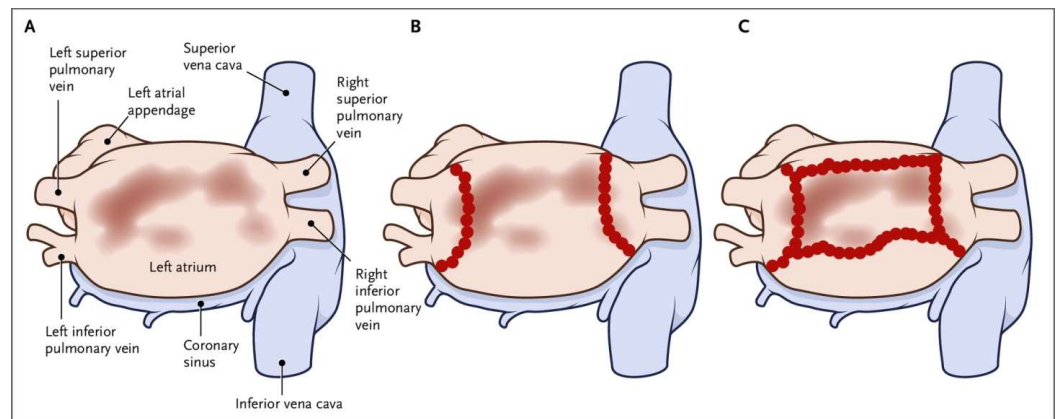


Tailored Afib ablation: Pisa approach

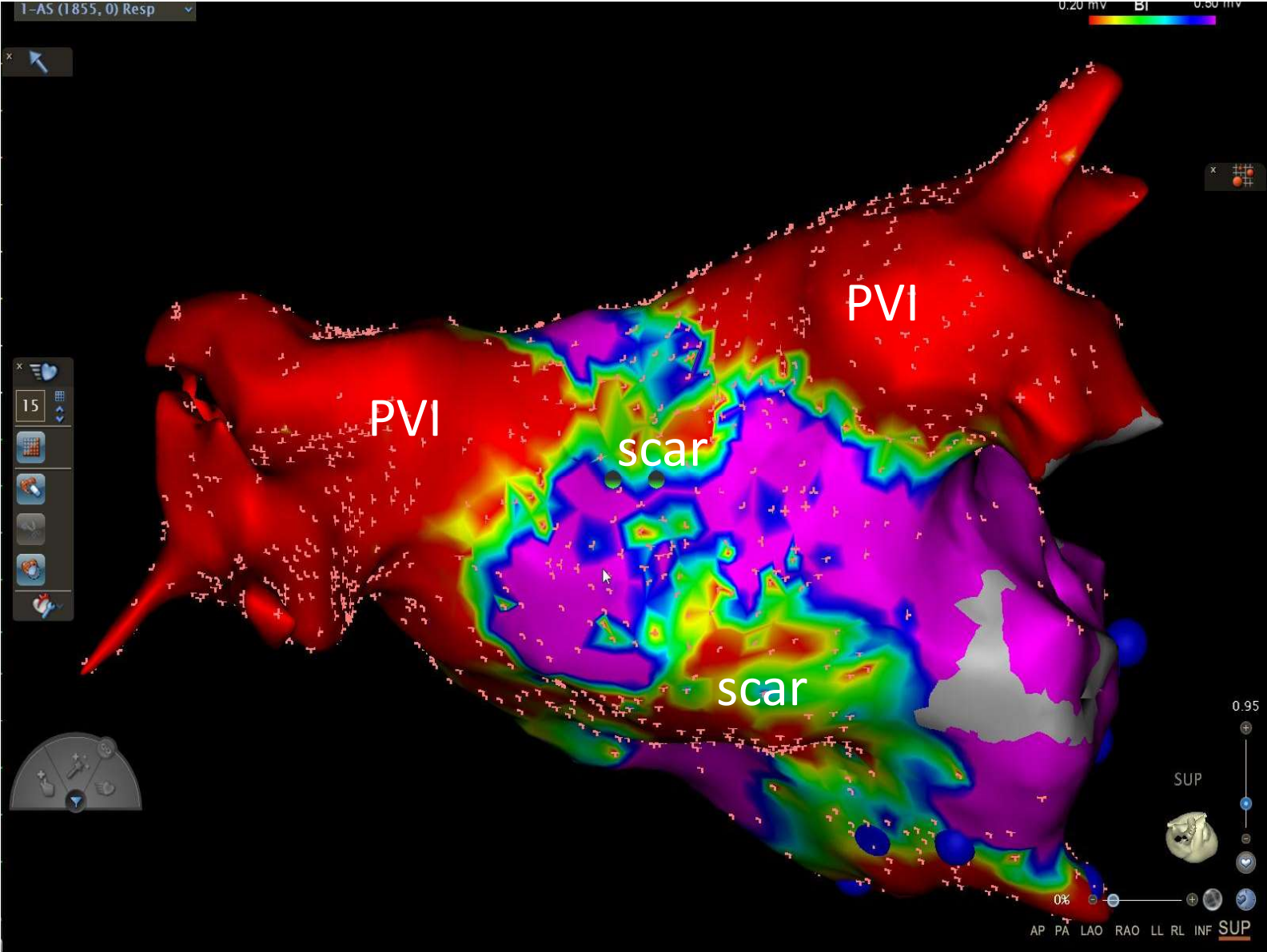


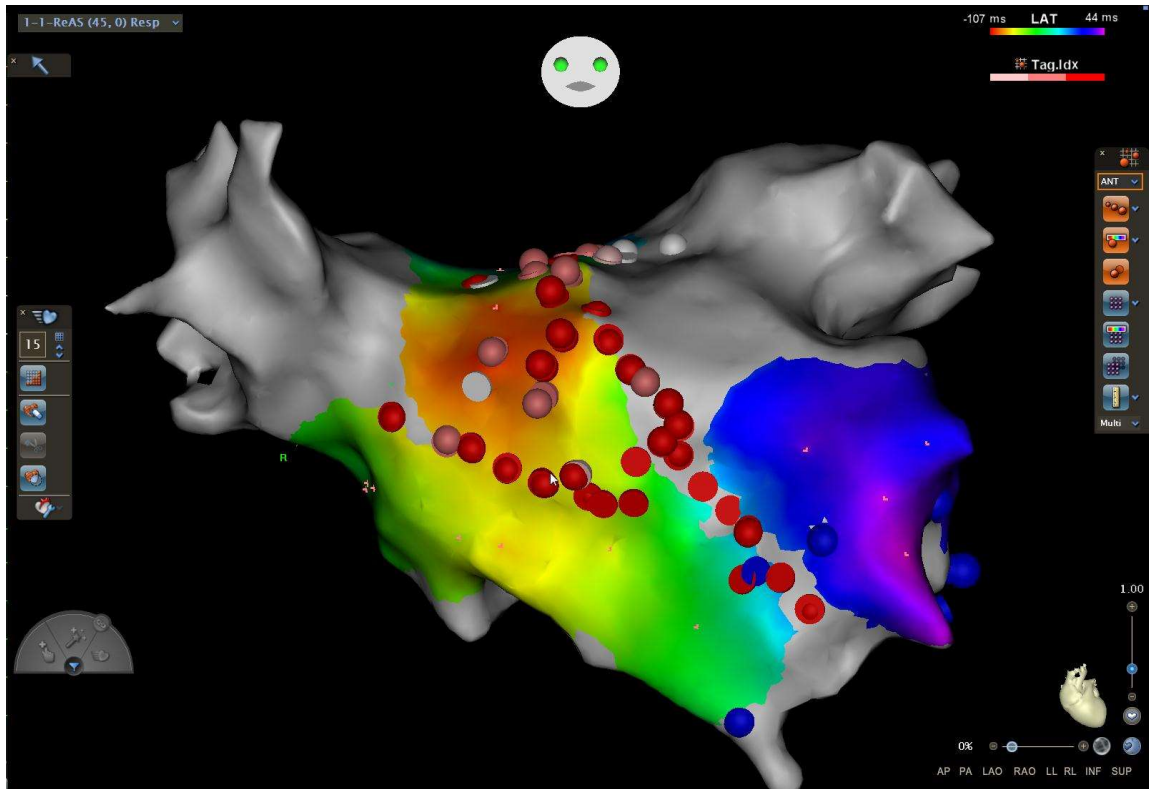
Low-Voltage Myocardium-Guided Ablation Trial of Persistent Atrial Fibrillation

Yan Huo, M.D., Ph.D.¹, Thomas Gaspar, M.D.¹, Robert Schönbauer, M.D.², Maciej Wójcik, M.D.³, Lukas Fiedler, M.D.^{4,5}, Franz Xaver Roithinger, M.D.⁴, Martin Martinek, M.D.⁶, Helmut Pürerfellner, M.D.⁶, Bettina Kirsstein, M.D.⁷, Utz Richter, M.D.¹, ...
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PVI + individualized ablation of atrial low-voltage myocardium significantly improved outcomes in patients with persistent AF





Conclusioni

In caso di FA di recente insorgenza:

- Trattare subito con controllo del ritmo
- Evitare di trattare solo i sintomatici
- Non aspettare troppo a fornire il trattamento più efficace (ablazione) sennò diventa persistente
- Se bassa EF prendere in considerazione la tachicardiomiopatia
- Nel dubbio se trattamento può essere efficace verificare se fibrosi con LGE



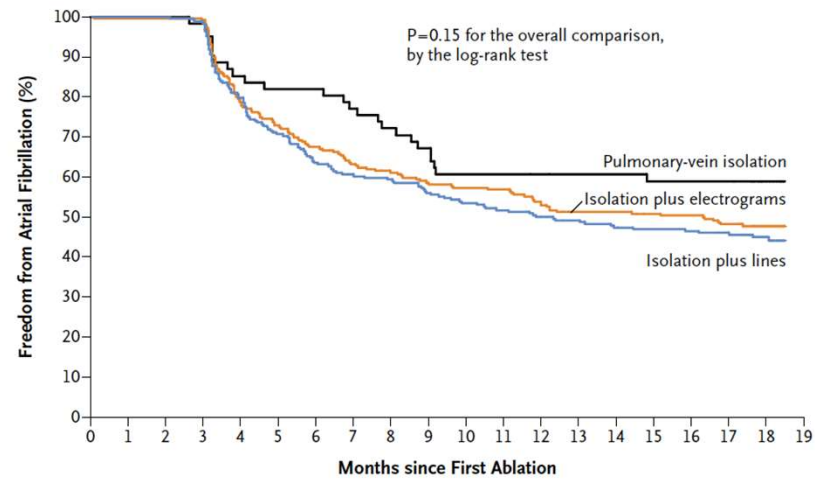
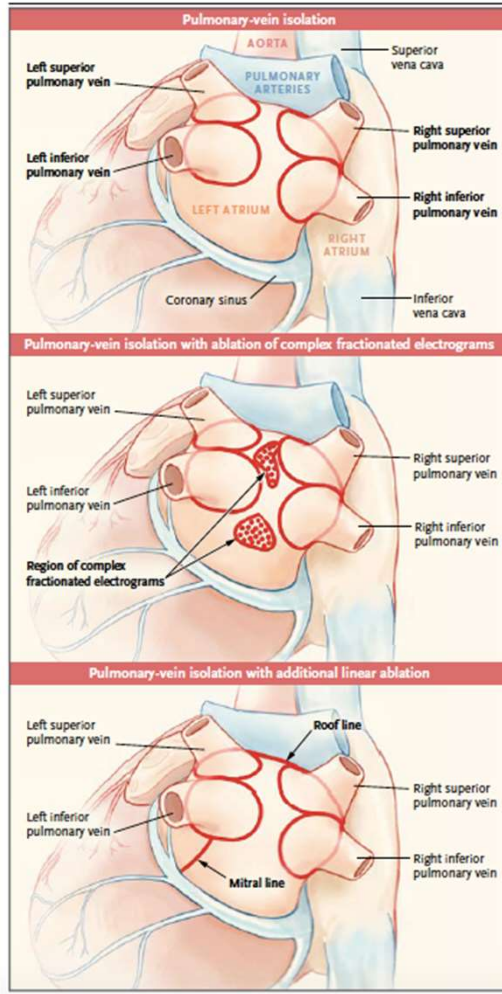
ITALIAN EP "SNIPERS"
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Other outcomes

Outcome	Early Rhythm Control	Usual Care	Treatment Effect
First primary outcome — events/person-yr (incidence/100 person-yr)	249/6399 (3.9)	316/6332 (5.0)	0.79 (0.66 to 0.94) [†]
Components of first primary outcome — events/person-yr (incidence/100 person-yr)			
→ <u>Death from cardiovascular causes</u>	67/6915 (1.0)	94/6988 (1.3)	0.72 (0.52 to 0.98) [‡]
→ <u>Stroke</u>	40/6813 (0.6)	62/6856 (0.9)	0.65 (0.44 to 0.97) [‡]
Hospitalization with worsening of heart failure	139/6620 (2.1)	169/6558 (2.6)	0.81 (0.65 to 1.02) [‡]
Hospitalization with acute coronary syndrome	53/6762 (0.8)	65/6816 (1.0)	0.83 (0.58 to 1.19) [‡]
Second primary outcome — nights spent in hospital/yr	5.8±21.9	5.1±15.5	1.08 (0.92 to 1.28) [§]
Key secondary outcomes at 2 yr			
Change in left ventricular ejection fraction — %	1.5±9.8	0.8±9.8	0.23 (−0.46 to 0.91) [¶]
Change in EQ-5D score	−1.0±21.4	−2.7±22.3	1.07 (−0.68 to 2.82) [¶]
Change in SF-12 Mental Score ^{**}	0.7±10.6	1.6±10.1	−1.20 (−2.04 to −0.37) [¶]
Change in SF-12 Physical Score ^{**}	0.3±8.5	0.1±8.2	0.33 (−0.39 to 1.06) [¶]
Change in MoCA score	0.1±3.3	0.1±3.2	−0.14 (−0.39 to 0.12) [¶]
Sinus rhythm — no. of patients with feature/total no. (%)	921/1122 (82.1)	687/1135 (60.5)	3.13 (2.55 to 3.84) ^{††}
<u>Asymptomatic — no. of patients with feature/total no. (%)^{‡‡}</u>	861/1159 (74.3)	850/1171 (72.6)	1.14 (0.93 to 1.40) ^{††}

AF Ablation: More is Less?



No. at Risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
Pulmonary-vein isolation	61	60	50	41	36																
Isolation plus electrograms	244	242	161	137	124																
Isolation plus lines	244	240	152	133	115																

Verma et al. STAR AF II. NEJM 2015; 372: 1812-22

- if patients managed their risk factors aggressively and achieved >10% weight-loss, 88% of patients initially with persistent AF reversed to either no AF or to paroxysmal AF

Europace 2018;20:1929–35

- As one of the first the Swedish ablation registry demonstrated a significantly reduced incidence of ischaemic stroke as well as mortality in 2496 patients after catheter ablation of AF as compared with the same number of patients without catheter ablation

Rate vs Rhythm control in HF

- Studies comparing rhythm and rate control in patients with AF and HF did not demonstrate benefit of medication-based rhythm control over rate control in terms of major clinical endpoints.²⁴ A recent meta-analysis comparing rhythm and rate control in a total of 2486 patients demonstrated comparable rates of mortality, stroke, and thromboembolic events between the two groups

LEGACY study

- First, there was a graded response with greater maintenance of sinus rhythm in those who had better control of their risk factors as measured by a weight-loss of $\geq 10\%$ (>5 -fold likelihood of maintaining sinus rhythm).
- Importantly, over 40% of the population who succeeded in achieving risk factor control and $\geq 10\%$ weight-loss maintained sinus rhythm without the use of rhythm control strategies.
- Second, this study was instrumental in demonstrating the negative impact of weight fluctuation on maintenance of sinus rhythm with important connotations for the development of dedicated AF programmes for risk factor management

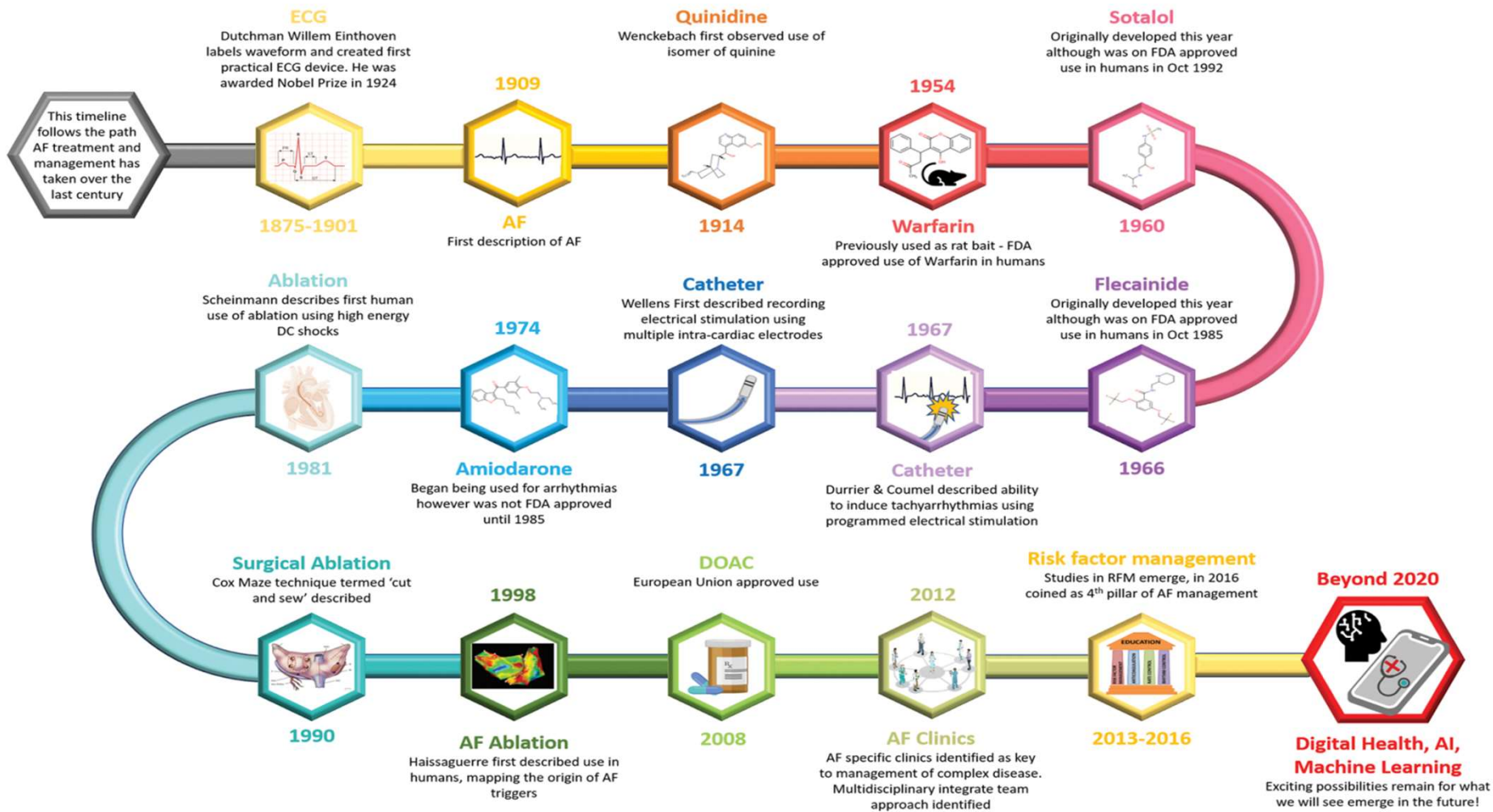
Others

- The CARDIO-FIT study expanded on these results demonstrating that there was an additive impact of improving cardiorespiratory fitness in the maintenance of sinus rhythm

J Am Coll Cardiol 2015;66:985–96

- Similarly, the ARREST-AF cohort study demonstrated that managing each risk factor aggressively was associated with a markedly improved success of catheter ablation procedures

J Am Coll Cardiol 2014;64:2222–31



7 landmark trials (Rhythm vs rate control)

- Use of antiarrhythmic drugs and withdrawal of anticoagulation (except for the PIAF trial) were the two treatment-related factors associated with mortality in the early randomized studies in pts with atrial fibrillation until 2020

Cardiovert & Forget



2000

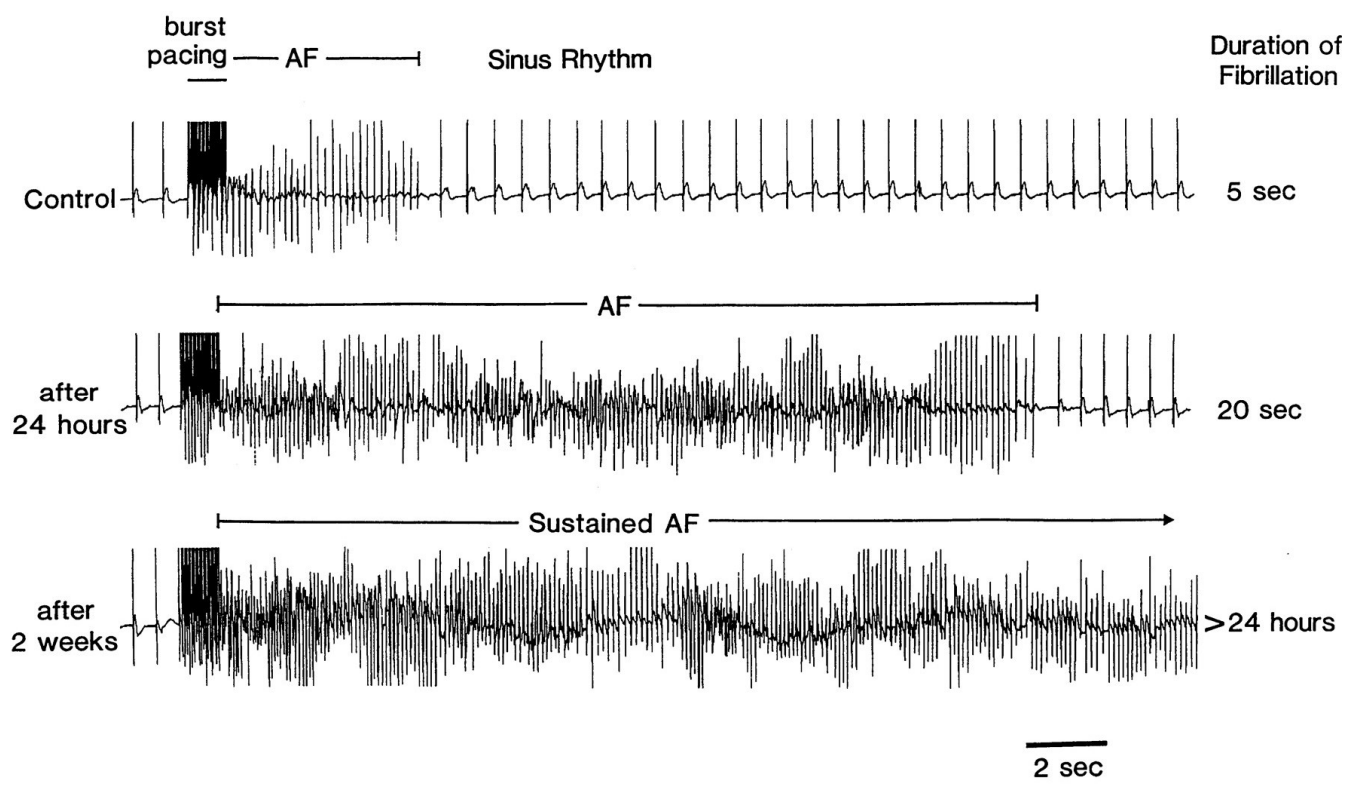
After Cardioversion, refrain from OAC resulting in increased prevalence of thromboembolic complications

Early vs Delayed treatment

- It has long been known that AF causes severe and longer-lasting atrial damage ('AF begets AF'), as one of the first, seminal papers was entitled*
- An early initiation of rhythm control therapy should make restoration and maintenance of SR more effective

*Wijffels, Allesie MA. Atrial fibrillation begets atrial fibrillation. A study in awake chronically instrumented goats. *Circulation* 1995 ;92:1954–6

Efficacy issue



*Wijffels, Allesie MA. Atrial fibrillation begets atrial fibrillation. A study in awake chronically instrumented goats. *Circulation* 1995 ;92:1954–6

Early vs Delayed treatment

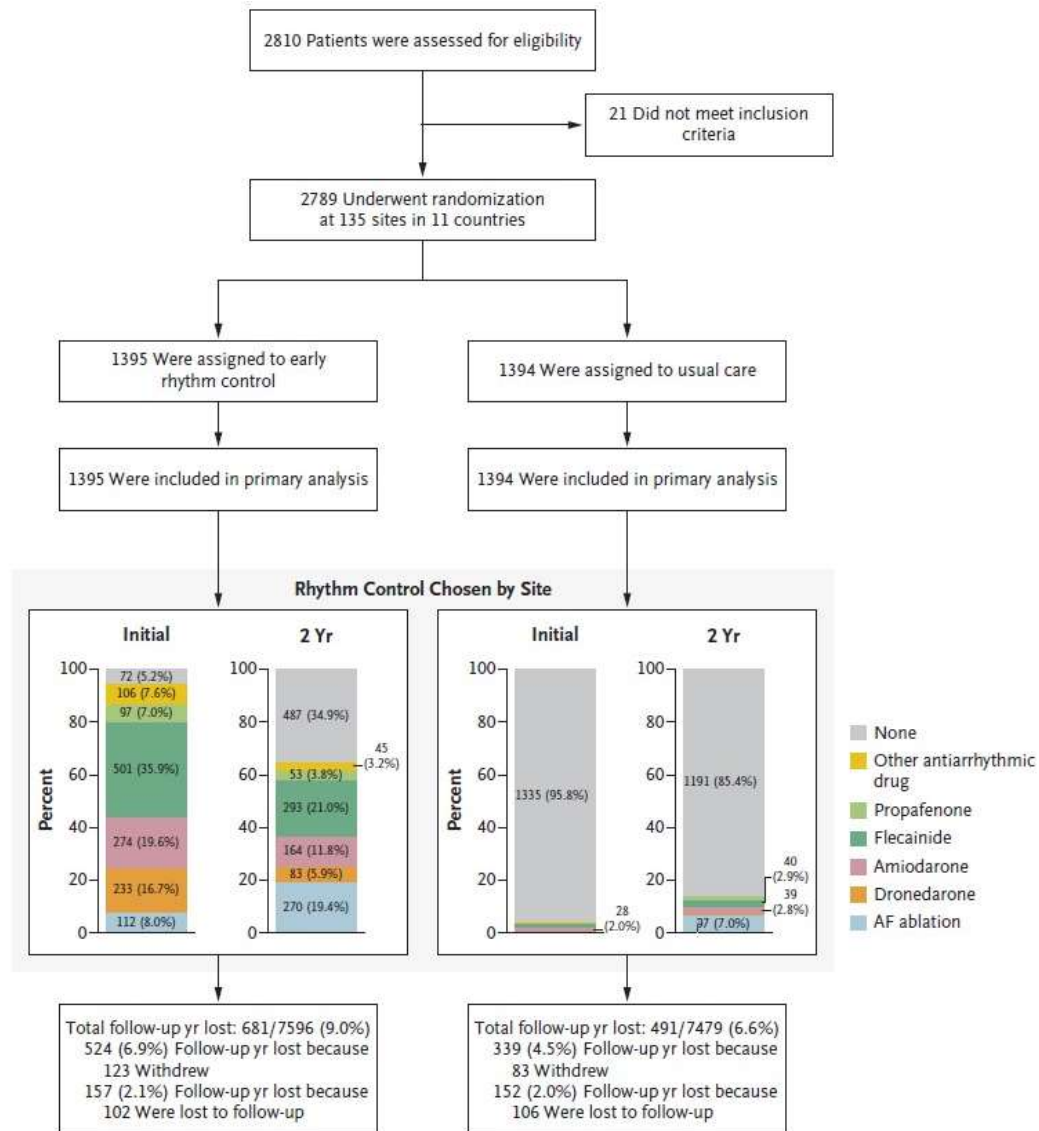
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*Wijffels, Allesie MA. Atrial fibrillation begets atrial fibrillation. A study in awake chronically instrumented goats. *Circulation* 1995 ;92:1954–6

Observation about “Early is better”

- two-third of patients enrolled into ATHENA* had their AF first diagnosed <12 months prior to enrolment, and almost three quarters were in SR at enrolment, while most patients enrolled into RACE were in AF at enrolment, and many had a long history of AF

*ATHENA trial showed that dronedarone reduced the incidence of hospitalization due to CV or death in patients with PAF/Pers AF compared with placebo



CARATT CLINICHE

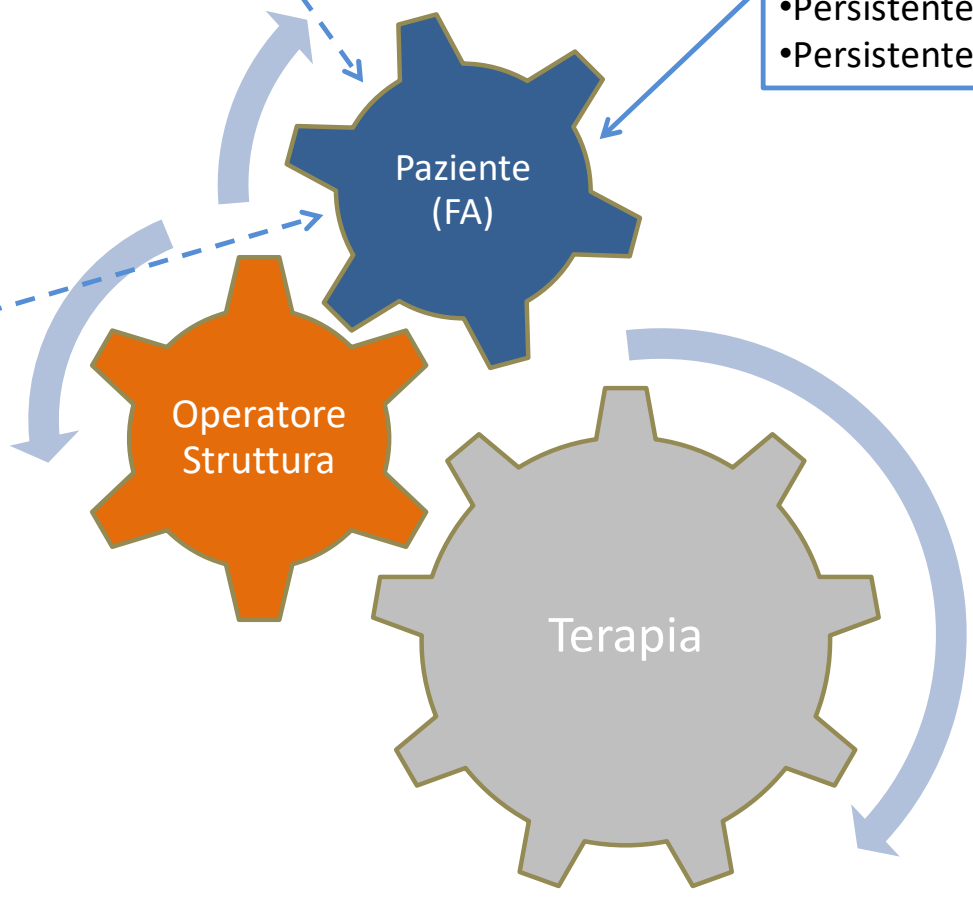
- età
- Comorbidità
- Cardiopatia strutturale?

Fibrillazione

- Parossistica
- Persistente
- Persistente long standing

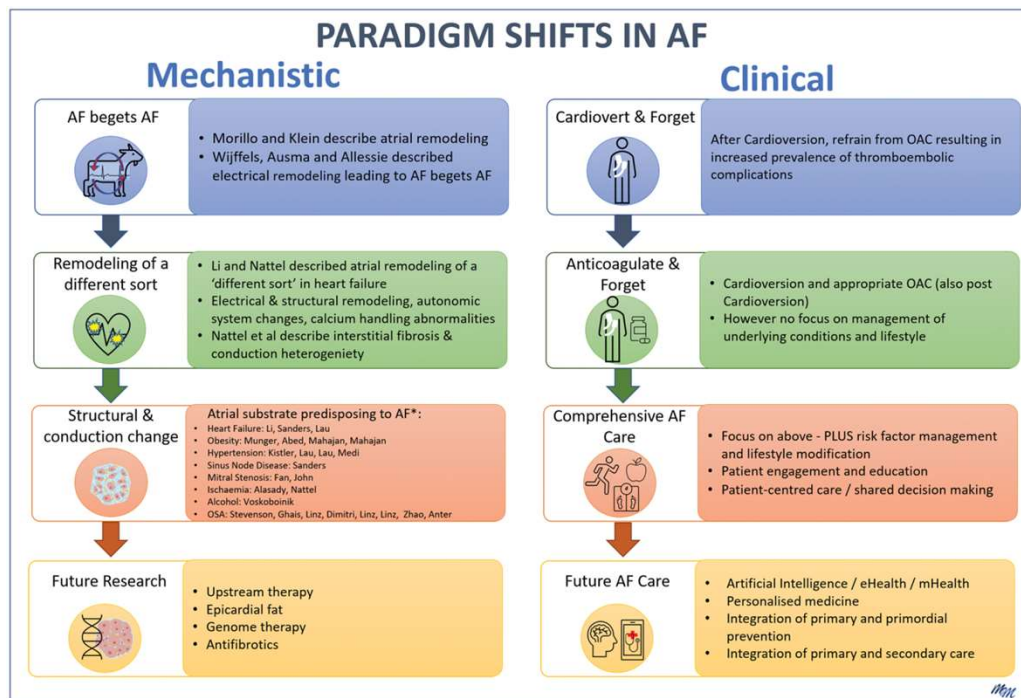
Caratteristiche Culturali/Psicologiche

- Percezione patologia
 1. Adeguata
 2. Eccessiva
 3. Scarsa
- Attesa nei confronti terapia



Risk Factor management

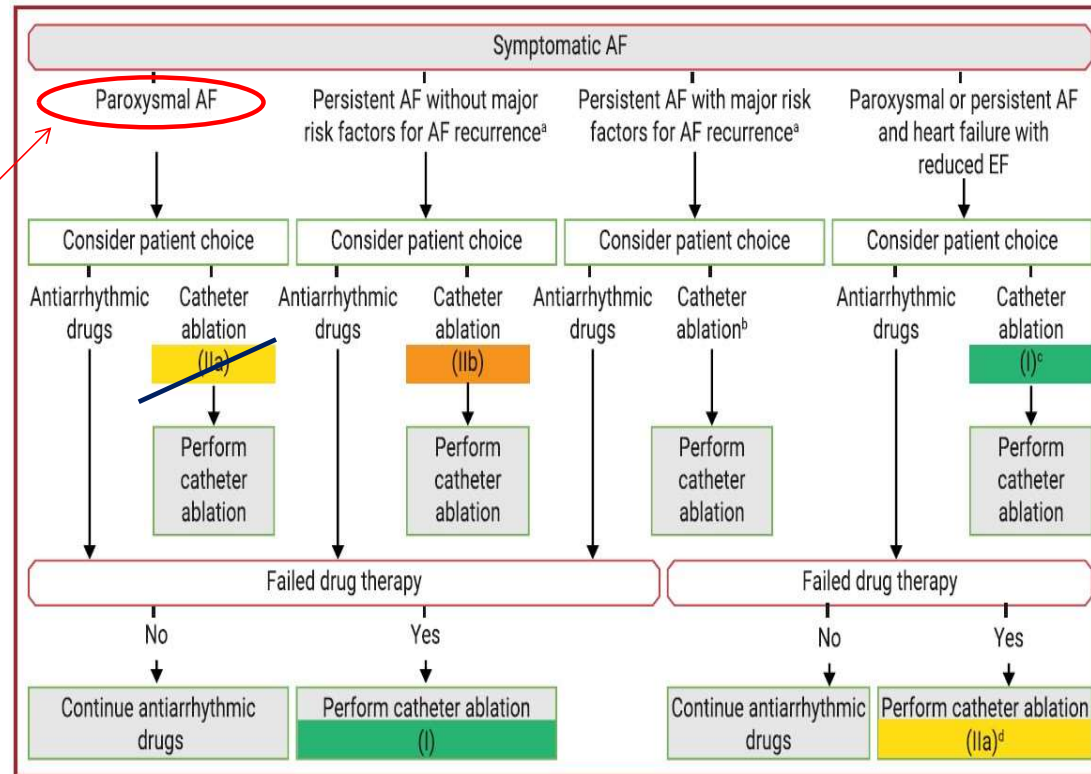
The 4th pillar



Check removable causes:
 Thyroid? OSAS? Pulmonary disease? Drugs

Control other causes:
 Pressure! Weight! Sedentary...

Paroxysmal atrial fibrillation



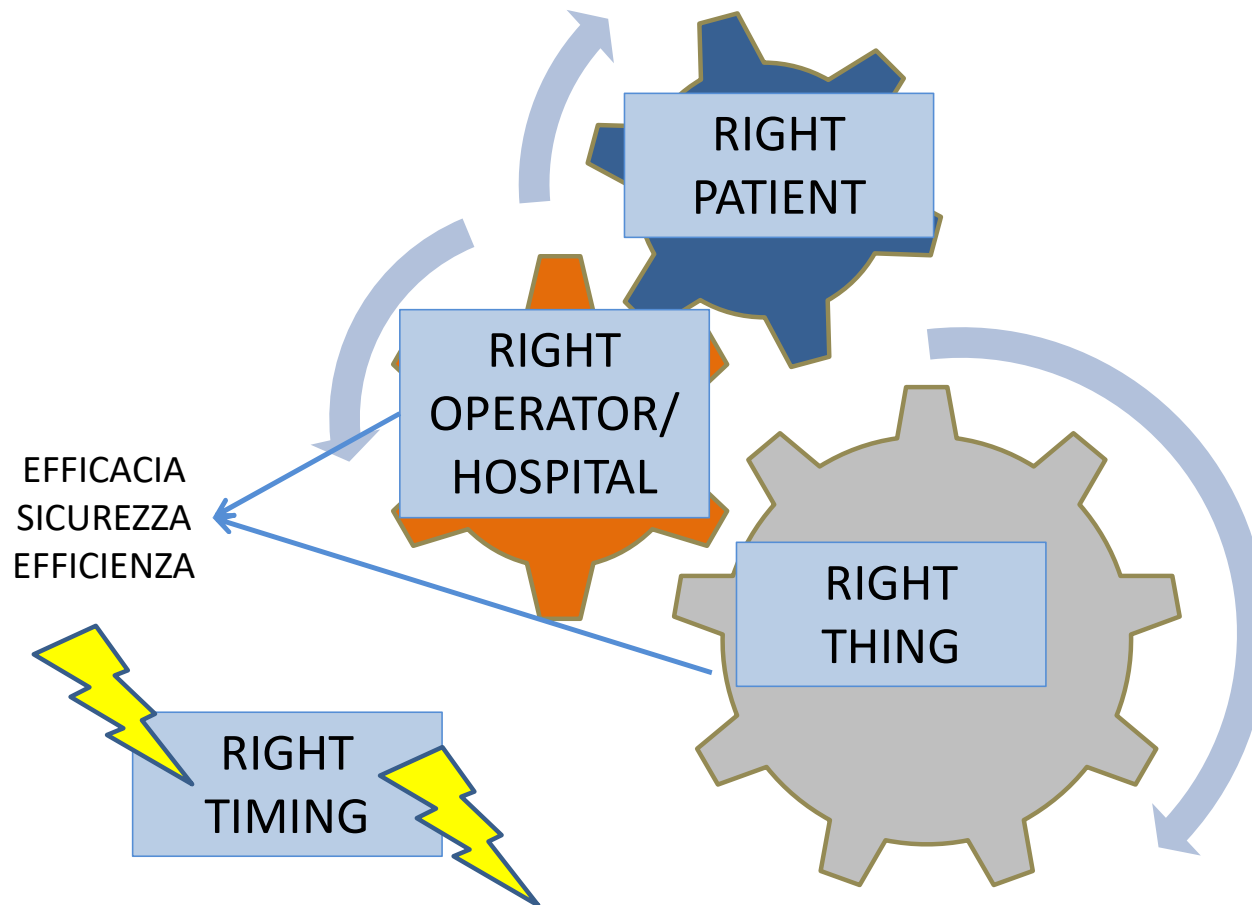
Ablation PAF
Next GL ??
First line
I class
LOE A



Quando PVI non funziona?

- Pazienti con atrio molto dilatato (cut-off?)
- Pazienti anziani (chi è anziano?)
- Donne (?)
- Pazienti con persistente di lunga data (>1 anno?)

Scelta Terapia della Fibrillazione atriale



PAF with symptoms

Non aspettare i sintomi



Guarda il burden!

