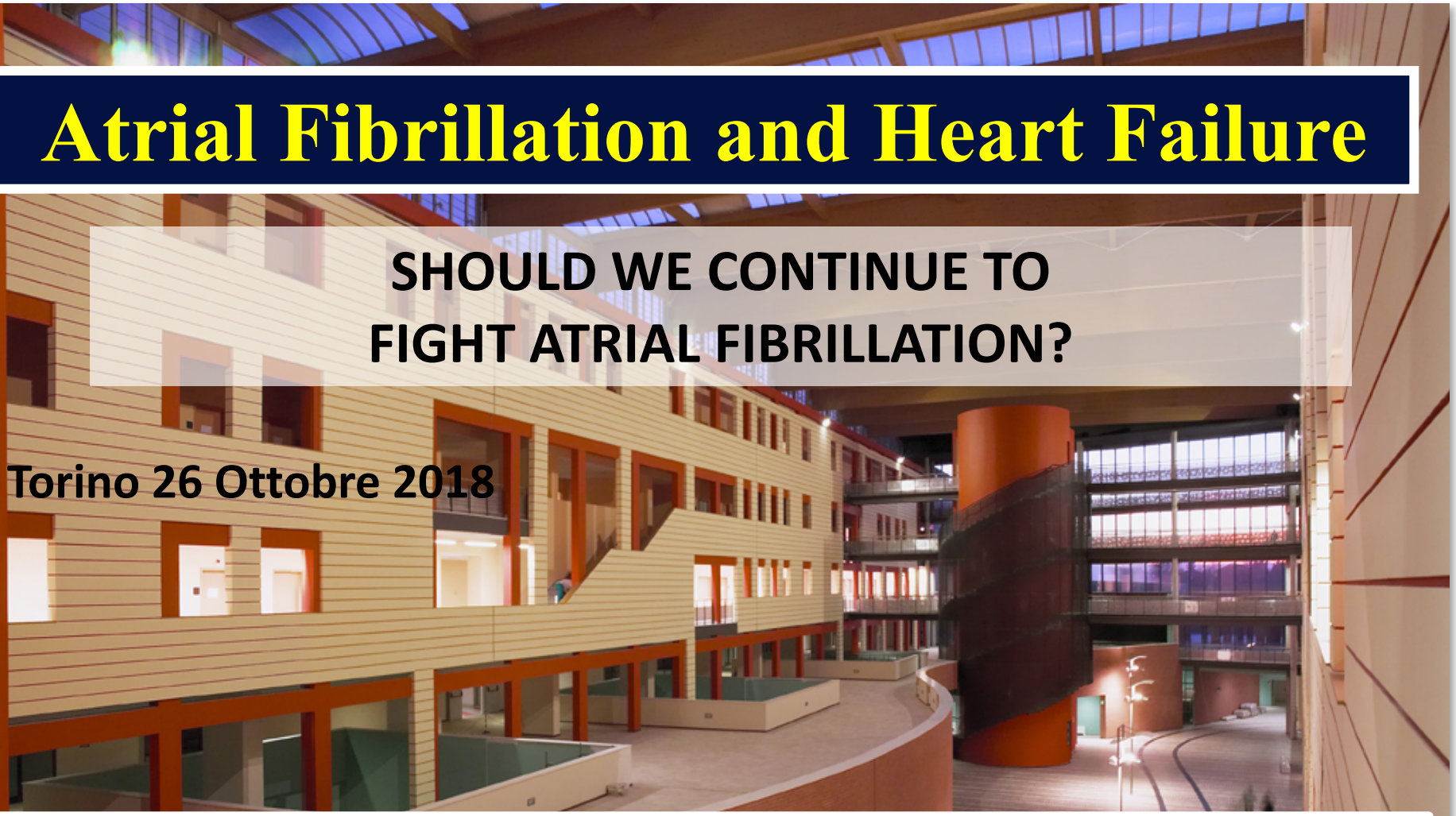
Atrial Fibrillation and Heart Failure

SHOULD WE CONTINUE TO FIGHT ATRIAL FIBRILLATION?

Torino 26 Ottobre 2018



Dr Marco Scaglione

Direttore S.C. Cardiologia

Ospedale Cardinal Massaia - Asti

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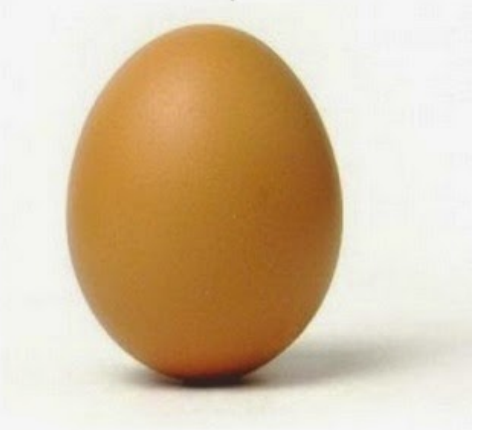
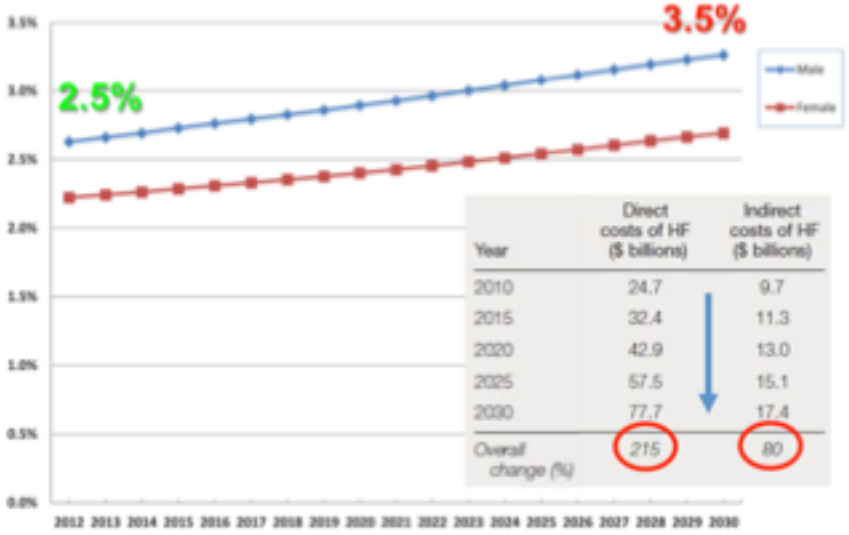


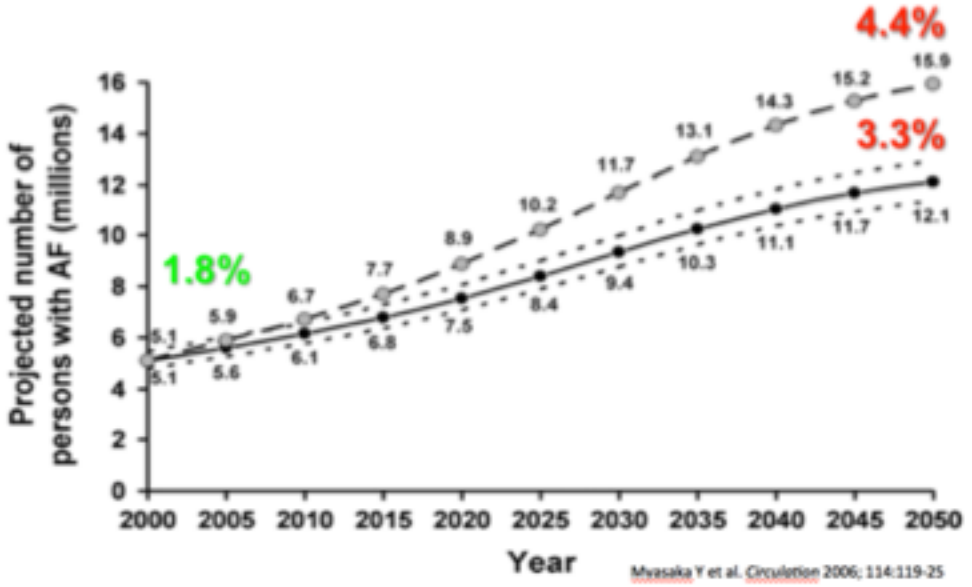
HF Epidemiology - Prevalence



Year	Direct costs of HF ($ billions)	Indirect costs of HF ($ billions)
2010	24.7	9.7
2015	32.4	11.3
2020	42.9	13.0
2025	57.5	15.1
2030	77.7	17.4
Overall change (%)	*215*	*80*

Heidenreich PA et al. *Circ Heart Fail* 2013; 6:606-

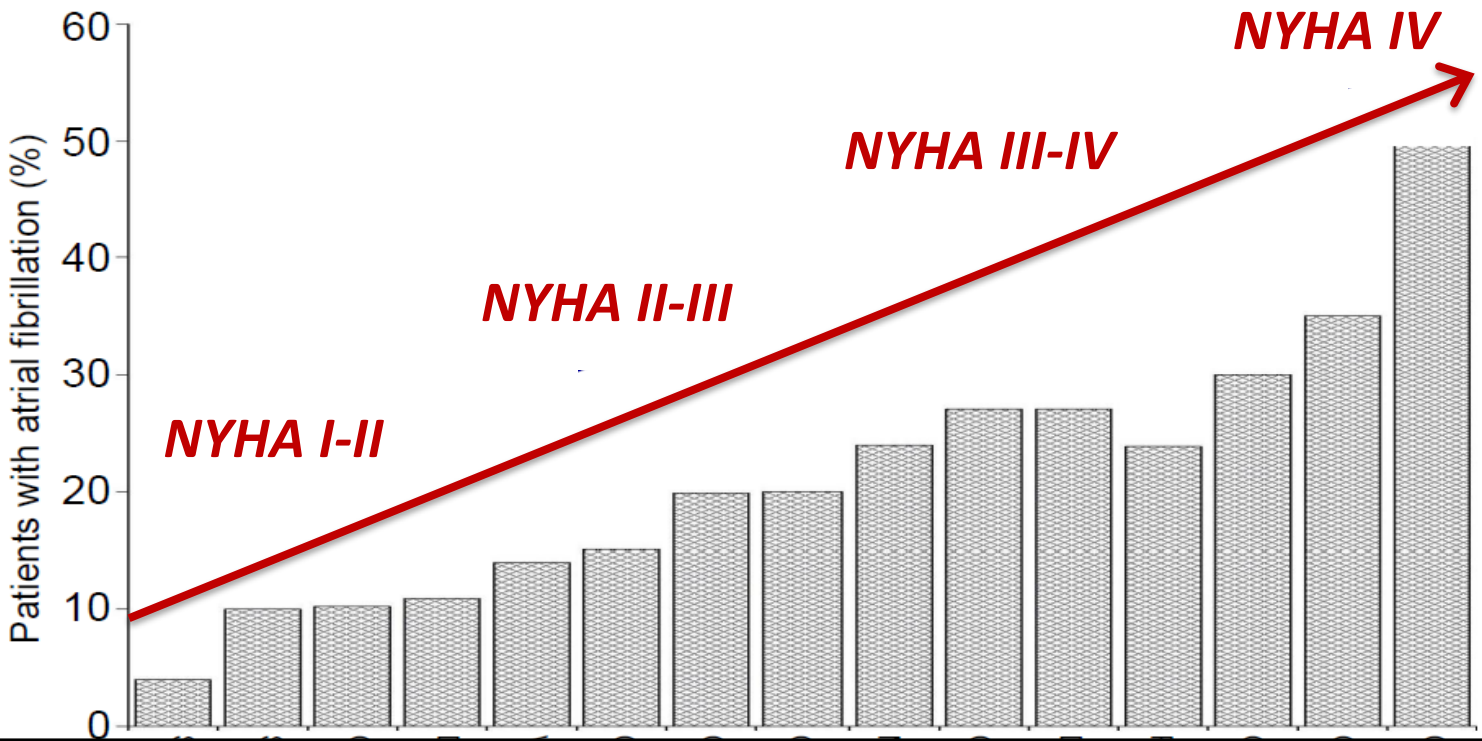
AF Epidemiology - Prevalence



Mvasaka Y et al. *Circulation* 2006; 114:119-25

How Often AF and HF Epidemics Collide?

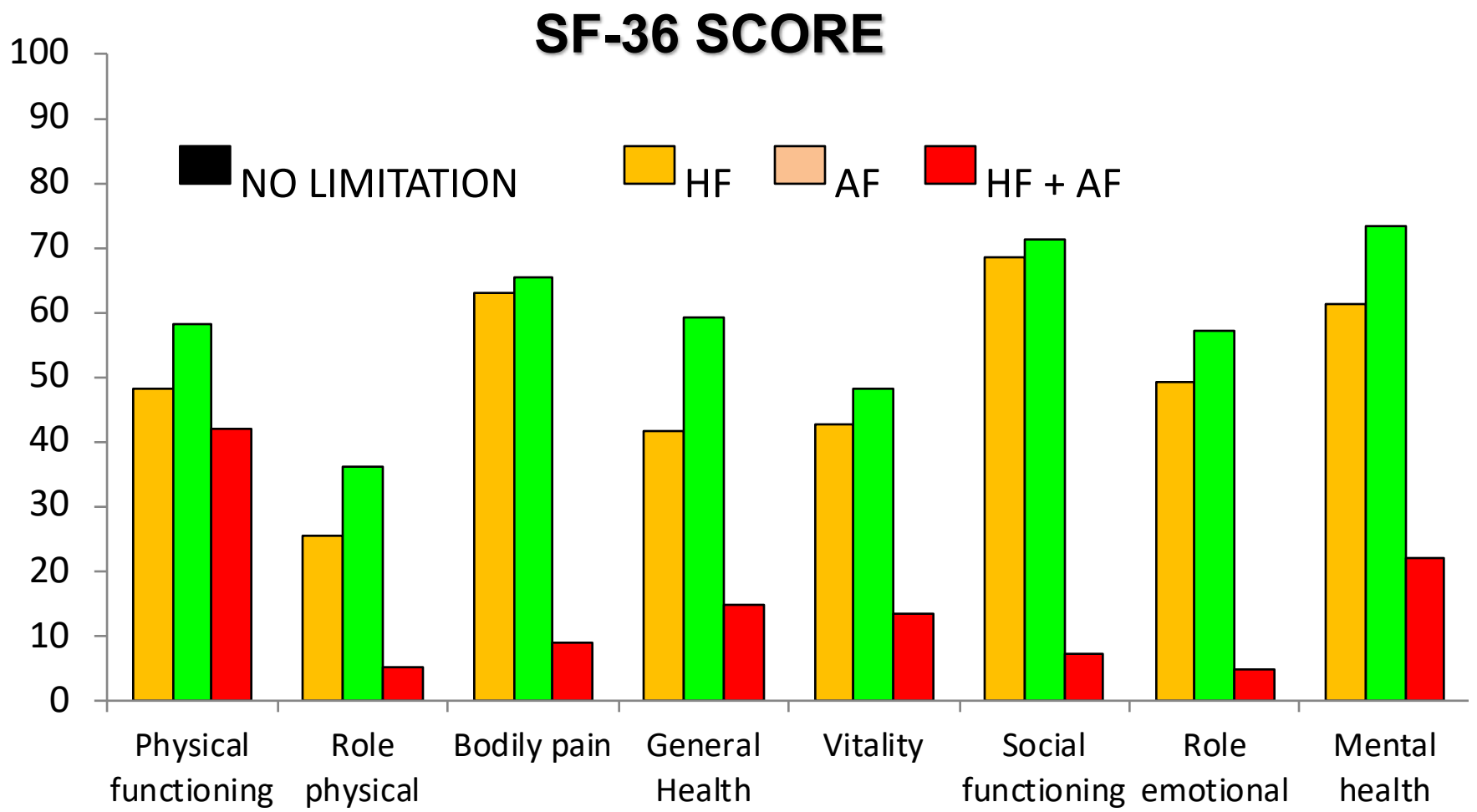
AF is estimated to occur in ≈30% of pts with HF



HF increases the risk of AF by a 4.5 factor in ♂ and 5.9 in ♀

Savelieva I et al. *Europace* 2004; 5: S5-S19

Impact of HF, AF and Both on QoL



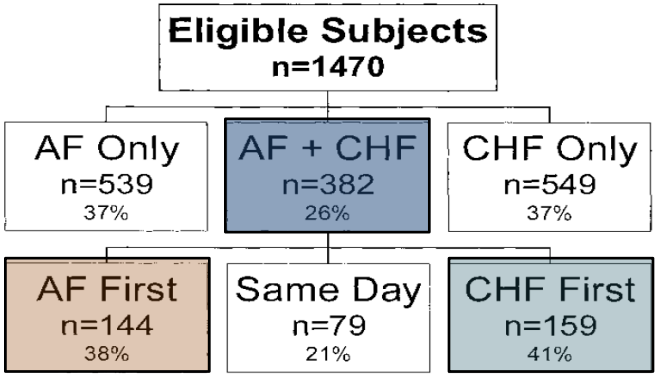
Juenger J et al. *Heart* 2002; 87: 235-241 AFFIRM Investigators *Am Heart* J 2005; 149:112- 20 Suman-Horduna I et al. *JACC* 2013; 61:455–60

Prognostic Impact of HF and AF

Temporal Relations of Atrial Fibrillation and Congestive Heart Failure and Their Joint Influence on Mortality

The Framingham Heart Study

Nei pz con sola FA o SC lo sviluppo della seconda condizione influenza negativamente la prognosi



Models	Men, Adjusted HR (95% CI)	Women, Adjusted HR (95% CI)
Comorbid condition as a time-dependent variable		
(A) Mortality after AF		
Impact of incident CHF	2.7 (1.9 to 3.7)*	3.1 (2.2 to 4.2)*
(B) Mortality after CHF		
Impact of incident AF	1.6 (1.2 to 2.1)†	2.7 (2.0 to 3.6)*

Wang J et al. *Circulation* 2003;107:2920-5

The interaction between HF and AF

Atrial Fibrillation

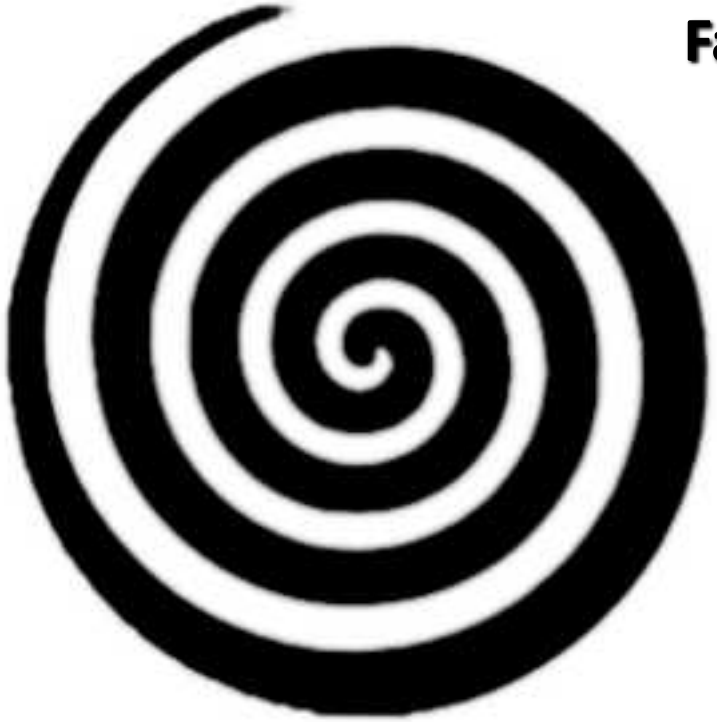
Triggered activity

Heterogeneous conduction

Atrial fibrosis

Atrial stretch

Pressure and volume overload



Fast ventricular rate

Irregular cycles

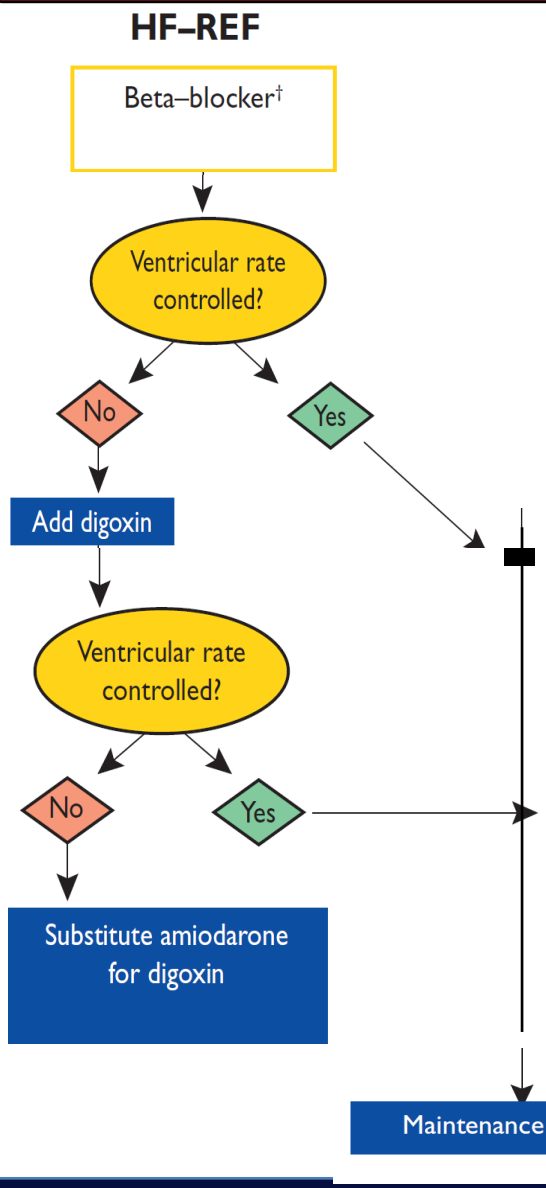
Loss of atrial contraction

Mitral and tricuspid regurgitation

Heart Failure

Rate Control in Patients with AF and HF

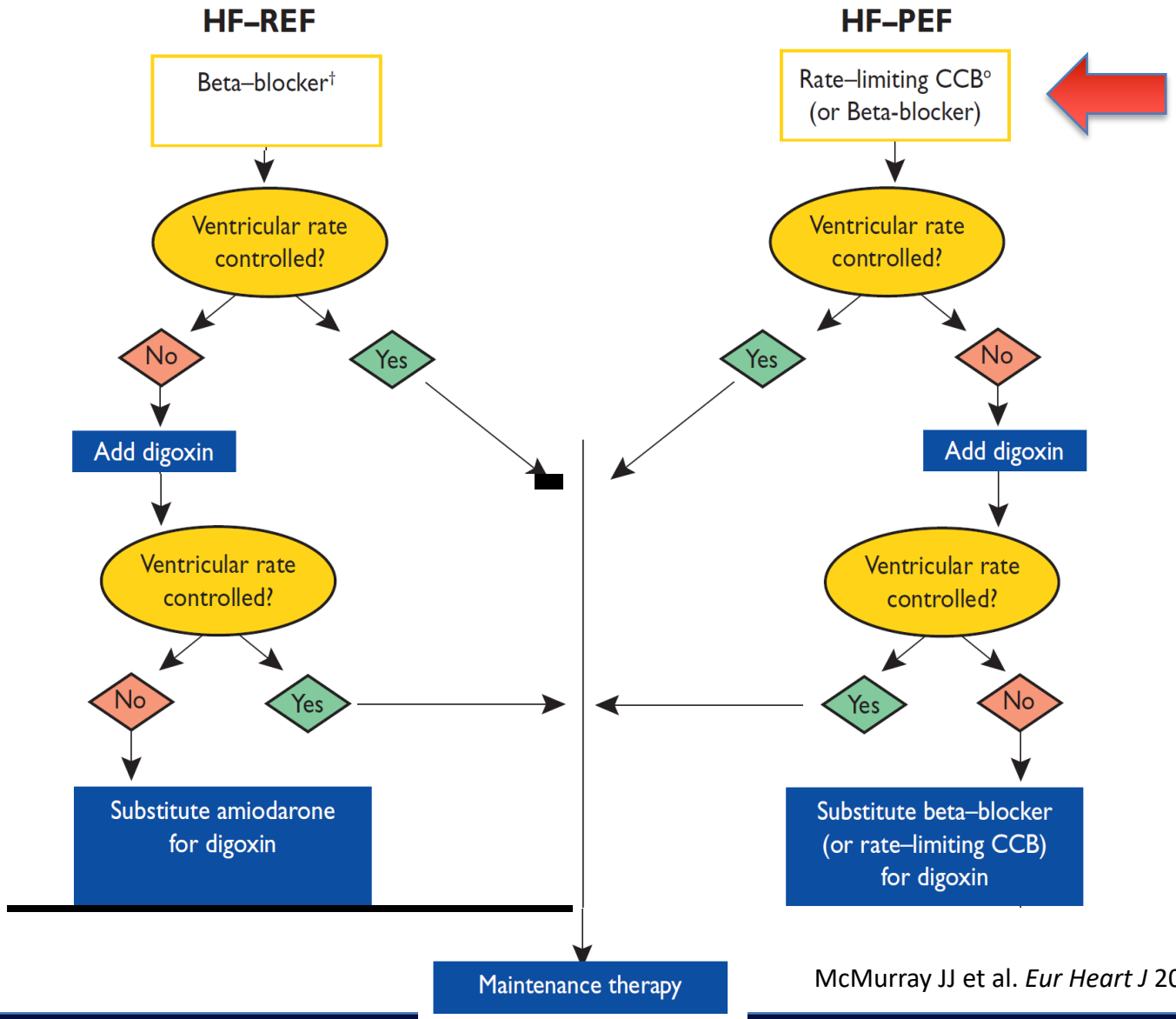
ESC HF guidelines 2012



Recommendations	Class[a]	Level[b]
Step 1: A beta-blocker		
A beta-blocker is recommended as the preferred first-line treatment to control the ventricular rate because of the associated benefits of this treatment (reducing the risk of hospitalization for worsening HF and reducing the risk of premature death).	I	A
Alternative Step 1 treatment		
(i) Digoxin is recommended in patients unable to tolerate a beta-blocker	I	B
(ii) Amiodarone may be considered in patients unable to tolerate a beta-blocker or digoxin.	IIb	C
Step 2: Digoxin		
Digoxin is recommended as the preferred second drug, in addition to a beta-blocker, to control the ventricular rate in patients with an inadequate response to a beta-blocker.	I	B
Alternative Step 2 treatment		
(i) Amiodarone may be considered in addition to either a beta-blocker or digoxin (but not both) to control the ventricular rate in patients with an inadequate response and unable to tolerate the combination of both a beta-blocker and digoxin.	IIb	C
No more than two of three of a beta-blocker, digoxin, and amiodarone (or any other drug suppressing cardiac conduction) should be considered because of the risk of severe bradycardia, third-degree AV block, and asystole.	IIa	C

McMurray JJ et al. *Eur Heart J* 2012; 33:1787-847

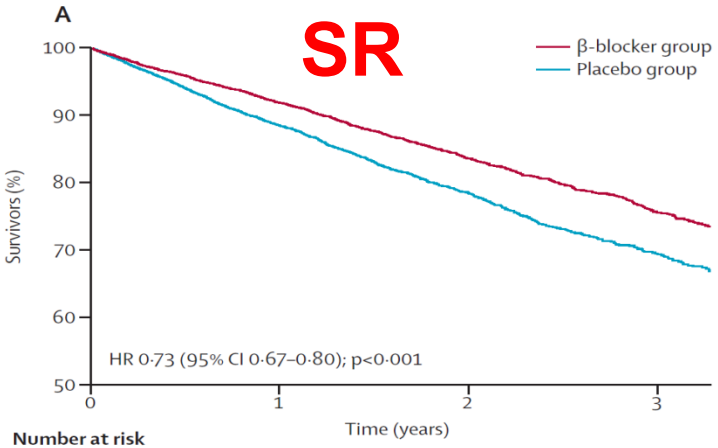
ESC HF guidelines 2012

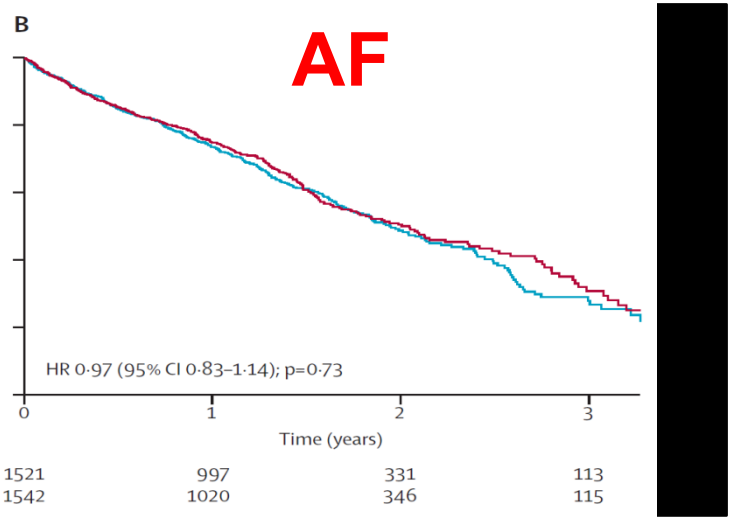


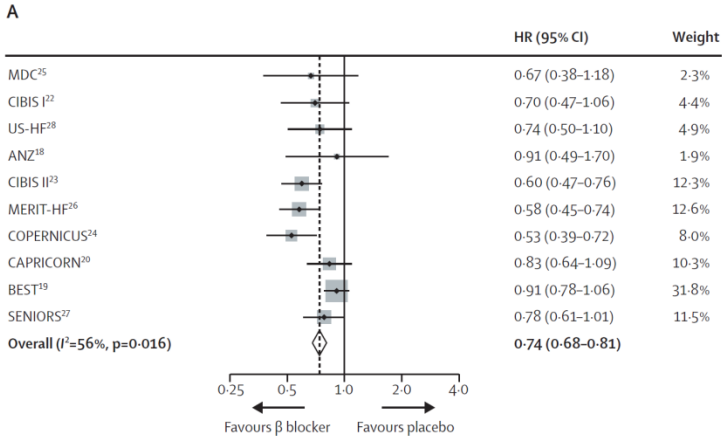
McMurray JJ et al. *Eur Heart J* 2012; 33:1787-847

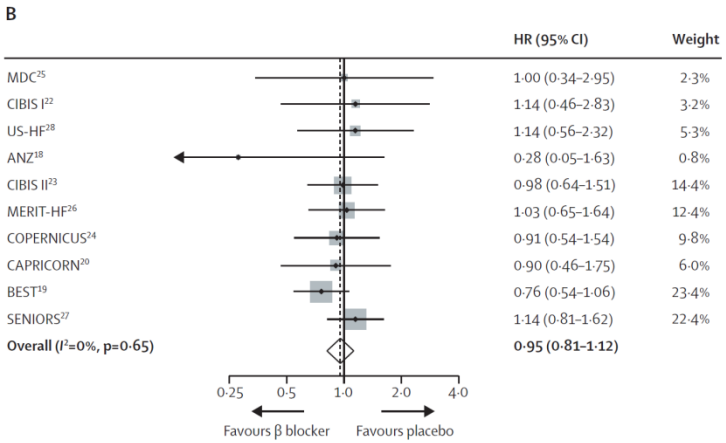
Efficacy of β blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis

Dipak Kotecha, Jane Holmes, Henry Krum, Douglas G Altman, Luis Manzano, John G F Cleland, Gregory Y H Lip, Andrew J S Coats, Bert Andersson, Paulus Kirchhof, Thomas G von Lueder, Hans Wedel, Giuseppe Rosano, Marcelo C Shibata, Alan Rigby, Marcus D Flather, on behalf of the Beta-Blockers in Heart Failure Collaborative Group



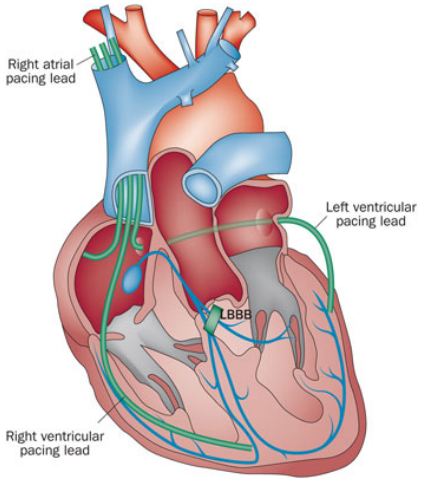






The Lancet, Published Online September 2, 2014

Non-Pharmacologic Rate Control



Management of AF in HF

Atrial Fibrillation

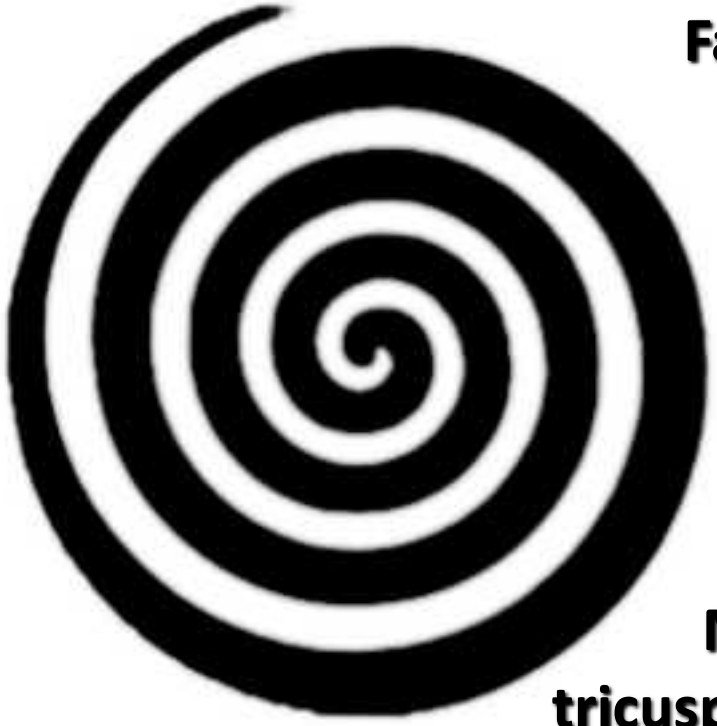
Triggered activity

Heterogeneous conduction

Atrial fibrosis

Atrial stretch

Pressure and volume overload



Fast ventricular rate

Irregular cycles

Loss of atrial contraction

Mitral and tricuspid regurgitation

Heart Failure

European Heart Journal (2008) **29**, 1644–1652
doi:10.1093/eurheartj/ehn133

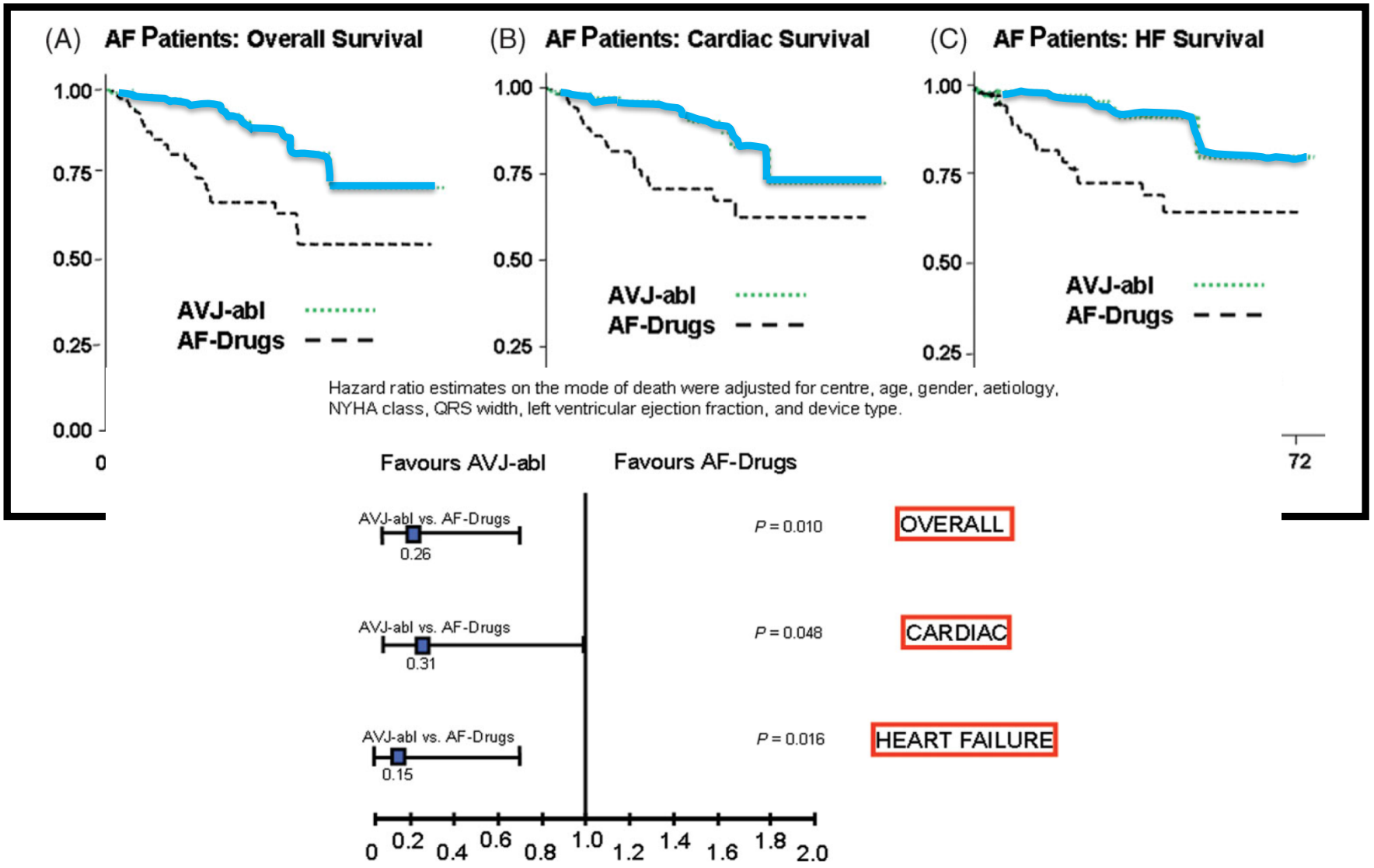
Long-term survival in patients undergoing cardiac resynchronization therapy: the importance of performing atrio-ventricular junction ablation in patients with permanent atrial fibrillation MILOS Study

- 1285 consecutive patients undergoing CRT
- 243 (19%) with permanent AF (19%)
- LVEF <35%, QRS >120 ms, NYHA > II
- Follow-up 34 months (10-40)
- BVP ≤ 85% at 2 months → AVJ ablation

1285 pts
1042 pts in SR
243 (19%) pts in AF
118 AV ablation
125 Pharmacological Tx
(50% ICD)

Gasparini et al. Eur Heart J 2008; 29:1644-1652

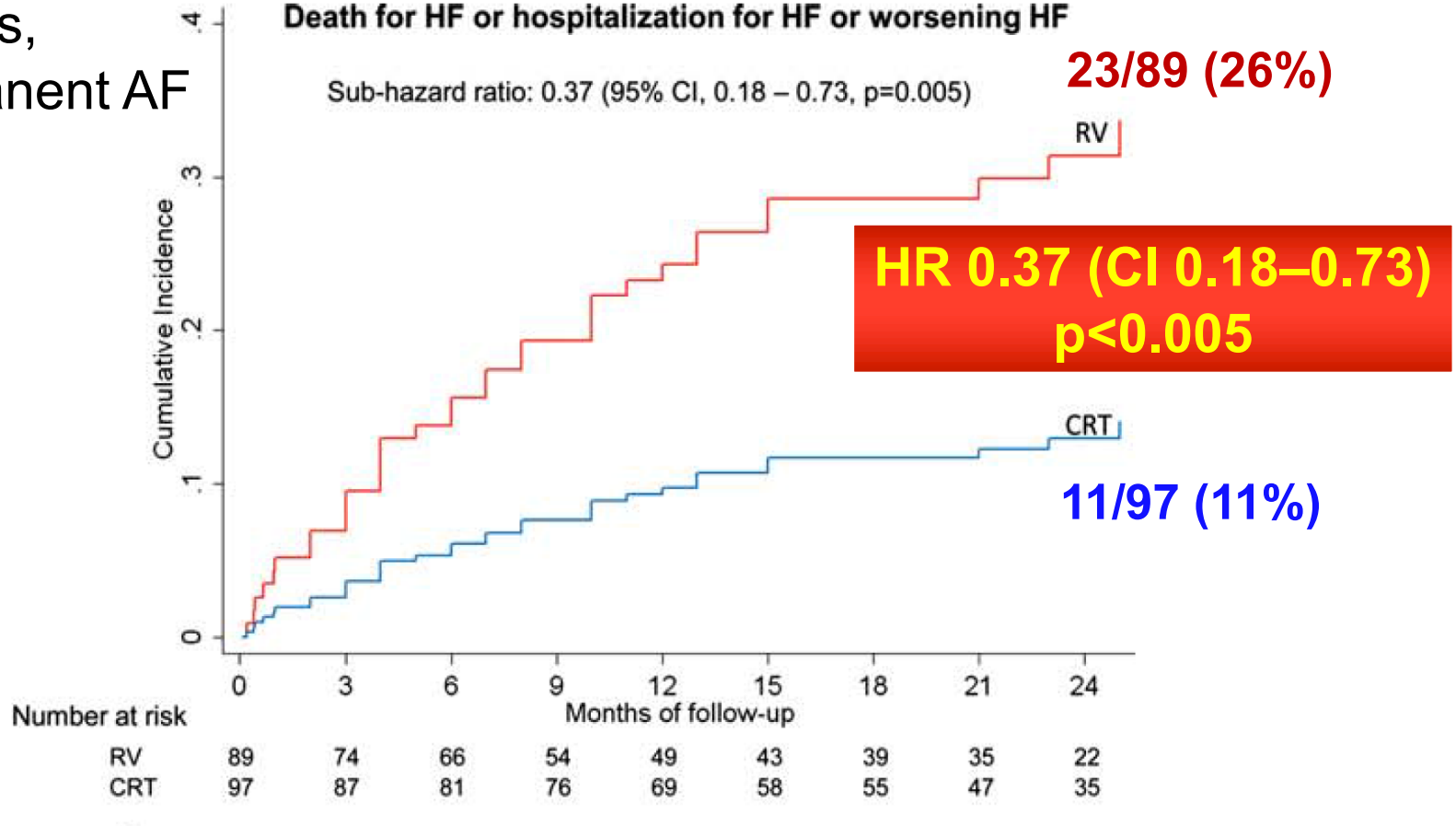
MILOS Study



Gasparini et al. Eur Heart J 2008; 29:1644-1652

Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial

186 pts,
Permanent AF
LVSD



Brignole M et al. *Eur Heart J* 2011; 32, 2420–2429

Rhythm Control in Patients with AF and HF

Management of AF in HF

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Triggered activity

Heterogeneous conduction

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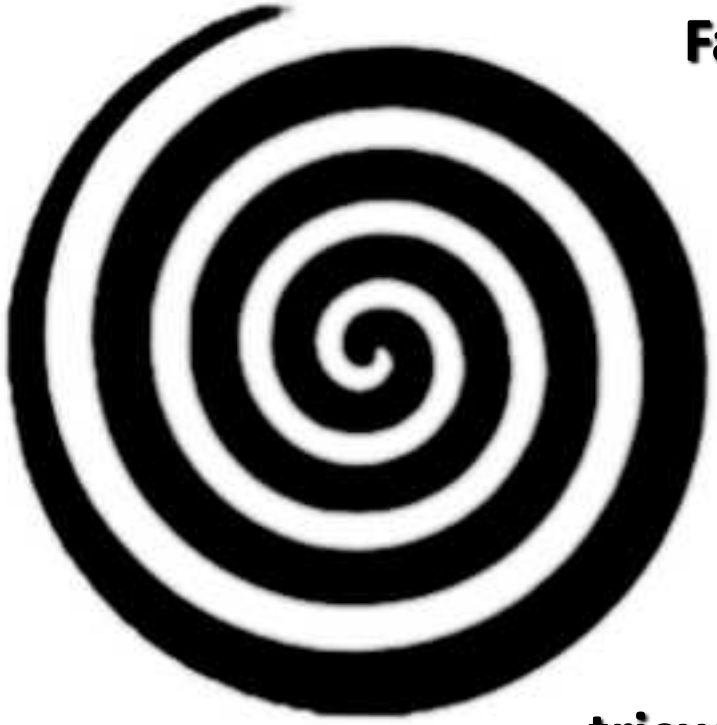
Pressure and volume overload



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Irregular cycles

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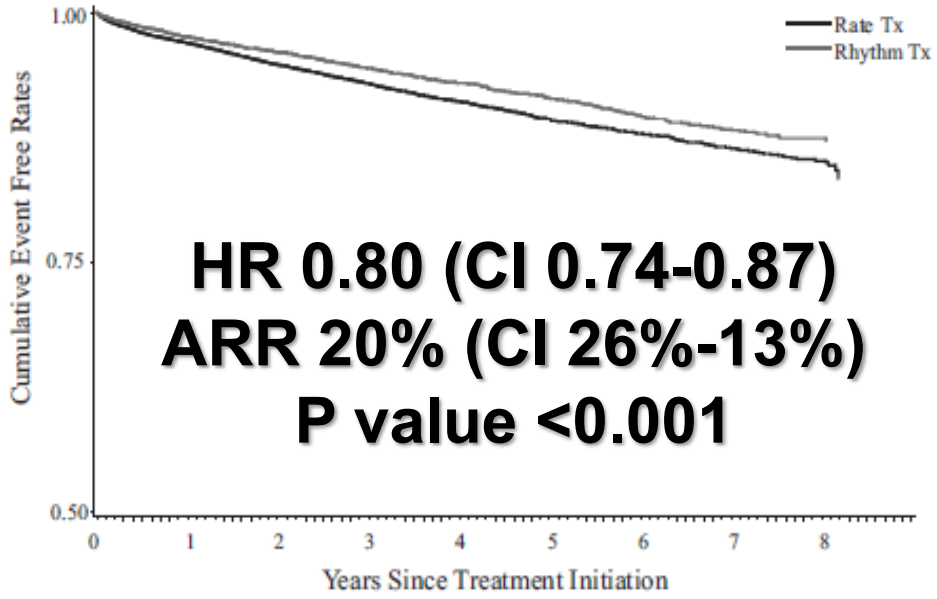
Heart Failure

Why Rhythm Control May Be Important

Rhythm Versus Rate Control Therapy and Subsequent Stroke or Transient Ischemic Attack in Patients With Atrial Fibrillation

Meytal Avgil Tsadok, Cynthia A. Jackevicius, Vidal Essebag, Mark J. Eisenberg, Elham Rahme, Karin H. Humphries, Jack V. Tu, Hassan Behlouli and Louise Pilote

- Population-based Canadian observational study
- **16,325 pts** rhythm control strategy vs. **41,193 pts** rate control strategy
- Same antithrombotic treatment (≅59% on OAT)
- ≅ **30%** of patients with **symptomatic HF**
- FUP: **2.8 years**, primary outcome **incidence of stroke/TIA** per 100 pts/yr



HR 0.80 (CI 0.74-0.87)
ARR 20% (CI 26%-13%)
P value <0.001

Circulation 2012;126:2680-87

AFFIRM: Total Mortality (at 5 years)

Rate control *vs* Rhythm control

Rate control + OAT *vs*. Rhythm control with AAD +/- OAT

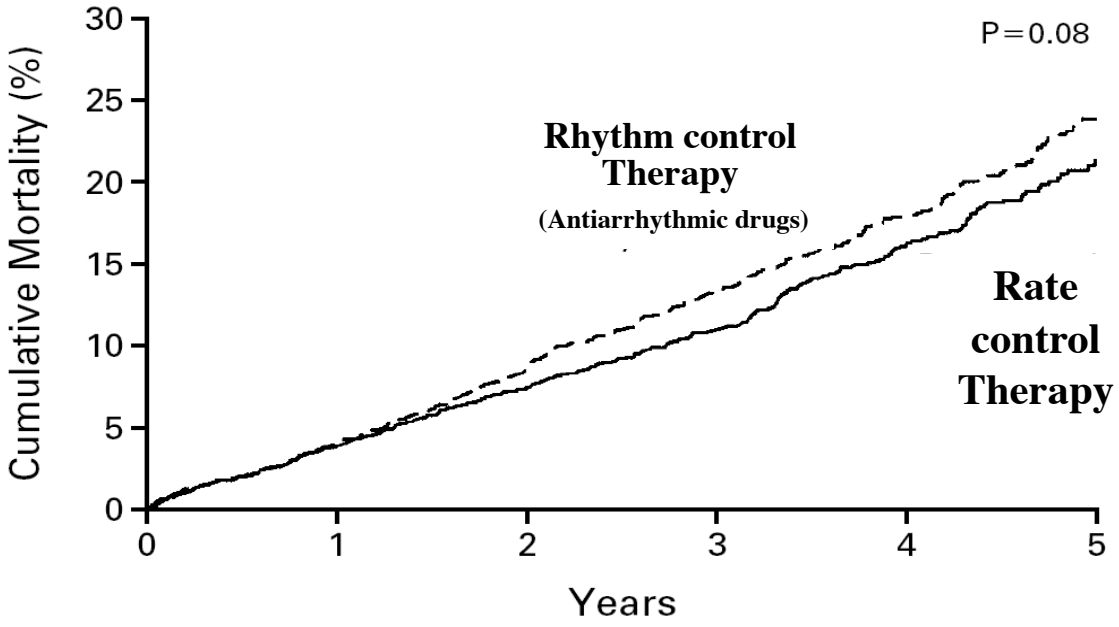
4060 pts,

Age 69.7±9 years

528 pts (13%) > 80 y

- 70.8% Hypertension
- 38.2% Ischemic
- ↓ EF 26%
- ↑ Left atrium 64.7%

Mean FU: 3,5 y



No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

New Engl. J. Med 2002;347:1825–1833

AFFIRM:

"On Treatment" analysis in a subgroup of 2796 pts

Covariate	*P*	HR	HR: 99% Confidence Limits Lower	Upper
Age at enrollment*	<0.0001	1.06	1.05	1.08
Coronary artery disease	<0.0001	1.56	1.20	2.04
Congestive heart failure	<0.0001	1.57	1.18	2.09
Diabetes	<0.0001	1.56	1.17	2.07
Stroke or transient ischemic attack	<0.0001	1.70	1.24	2.33
Smoking	<0.0001	1.78	1.25	2.53
Left ventricular dysfunction	0.0065	1.36	1.02	1.81
Mitral regurgitation	0.0043	1.36	1.03	1.80
Sinus rhythm	<0.0001	0.53	0.39	0.72
Warfarin use	<0.0001	0.50	0.37	0.69
Digoxin use	0.0007	1.42	1.09	1.86
Rhythm-control drug use	0.0005	1.49	1.11	2.01

*Per year of age.

Corley SD et al. Circulation 2004; 109:1509-13

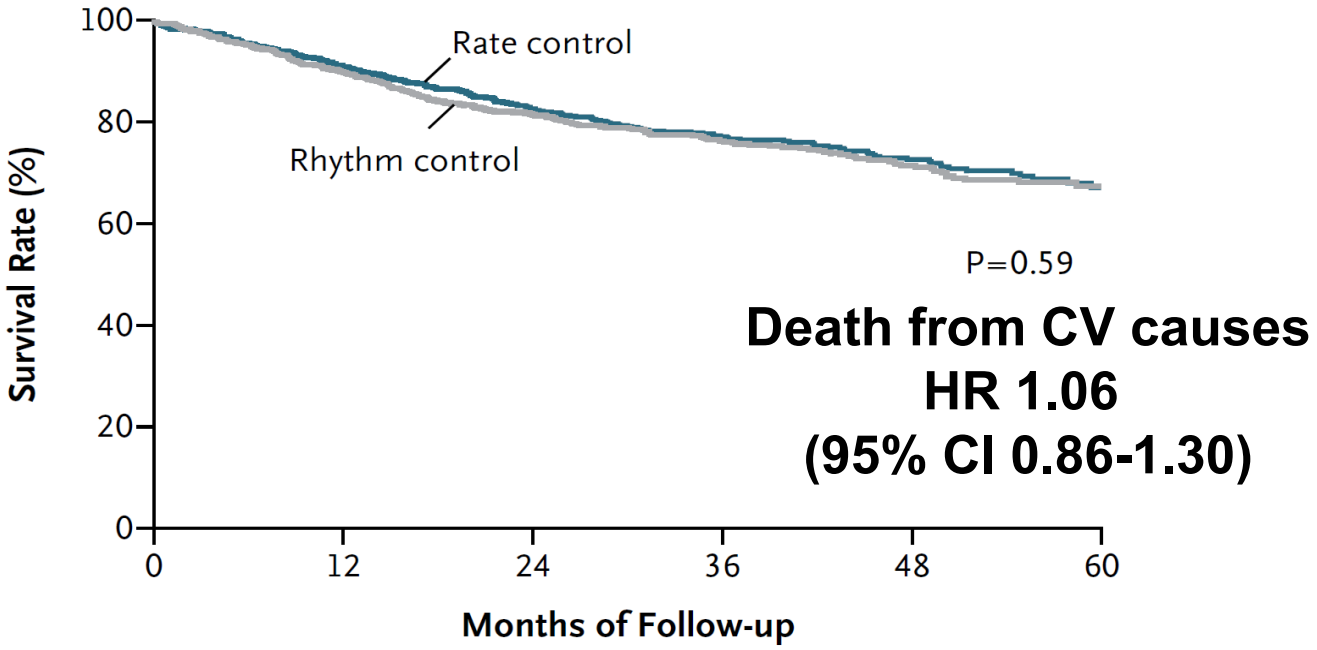
Rhythm (AAD ± CVE) vs. rate control trials

Trial	Inclusion criteria	Primary outcome Parameter	Patients reaching primary outcome (n)		
			Rate ctrl	Rhytm ctrl	P
PIAF (2000) 252 Patients	Persistent AF (7-360 days)	Symptomatic improvement	76/125 (60.8%)	70/127 (55.1%)	0.32
AFFIRM (2002) 4060 Patients	Paroxysmal AF or persistent AF, age ≥65 years, or risk of stroke or death	All-cause mortality	310/2027 (25.9%)	356/2033 (26.7%)	0.08
RACE (2002) 522 Patients	Persistent AF or flutter for <1 year and 1-2 cardioversions over 2 years and oral anticoagulation	Composite: cardiovascular death, CHF, severe bleeding, pacemaker implantatation, thrombo-embolic events, severe adverse effects of antiarrhythmic drugs	44/256 (17.2%)	60/266 (22.6%)	0.11
STAF (2003) 200 Patients	Persistent AF (>4 weeks and <2 years), LA size >45 mm, CHF NYHA II-IV, LVEF <45%	Composite: overall mortality, cerebrovascular complications, CPR, embolic events	10/100 (10.0%)	9/100 (9.0%)	0.99
HOT CAFÈ (2004) 205 Patients	First clinically overt persistent AF (≥7 days and <2 years), age 50-75 years	Composite: death, thrombo-embolic events; intracranial/major haemorrhage	1/101 (1.0%)	4/104 (3.9%)	>0.71
AF-CHF (2008) 1376 Patients	LVEF ≤35%, symptoms of CHF, history of AF (≥6 h or DCC <last 6 months)	Cardiovascular death	175/1376 (25%)	182/1376 (27%)	0.59
J-RHYTHM (2009) 823 Patients	Paroxysmal AF	Composite of total mortality, symptomatic cerebral infarction, systemic embolism, major bleeding, hospitalization for heart failure, or physical/psychological disability	89/405 (22.0%)	64/418 (15.3%)	0.012

AF-CHF Study

1376 patients with at least one episode of AF within 6 months:

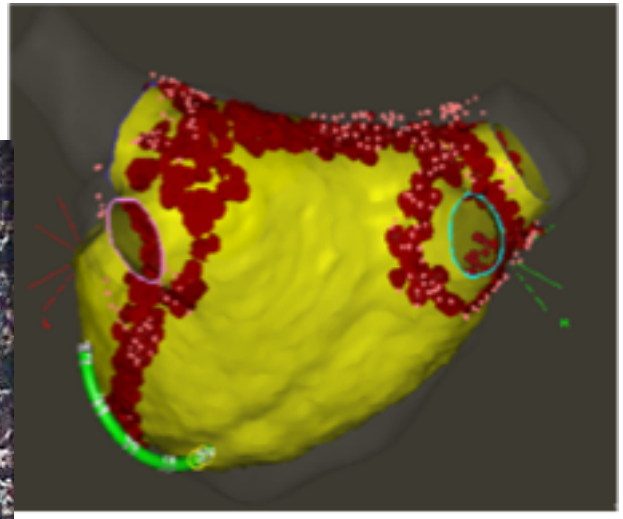
- LVEF ≤35%, NYHA II to IV
- LVEF ≤25%, asymptomatic



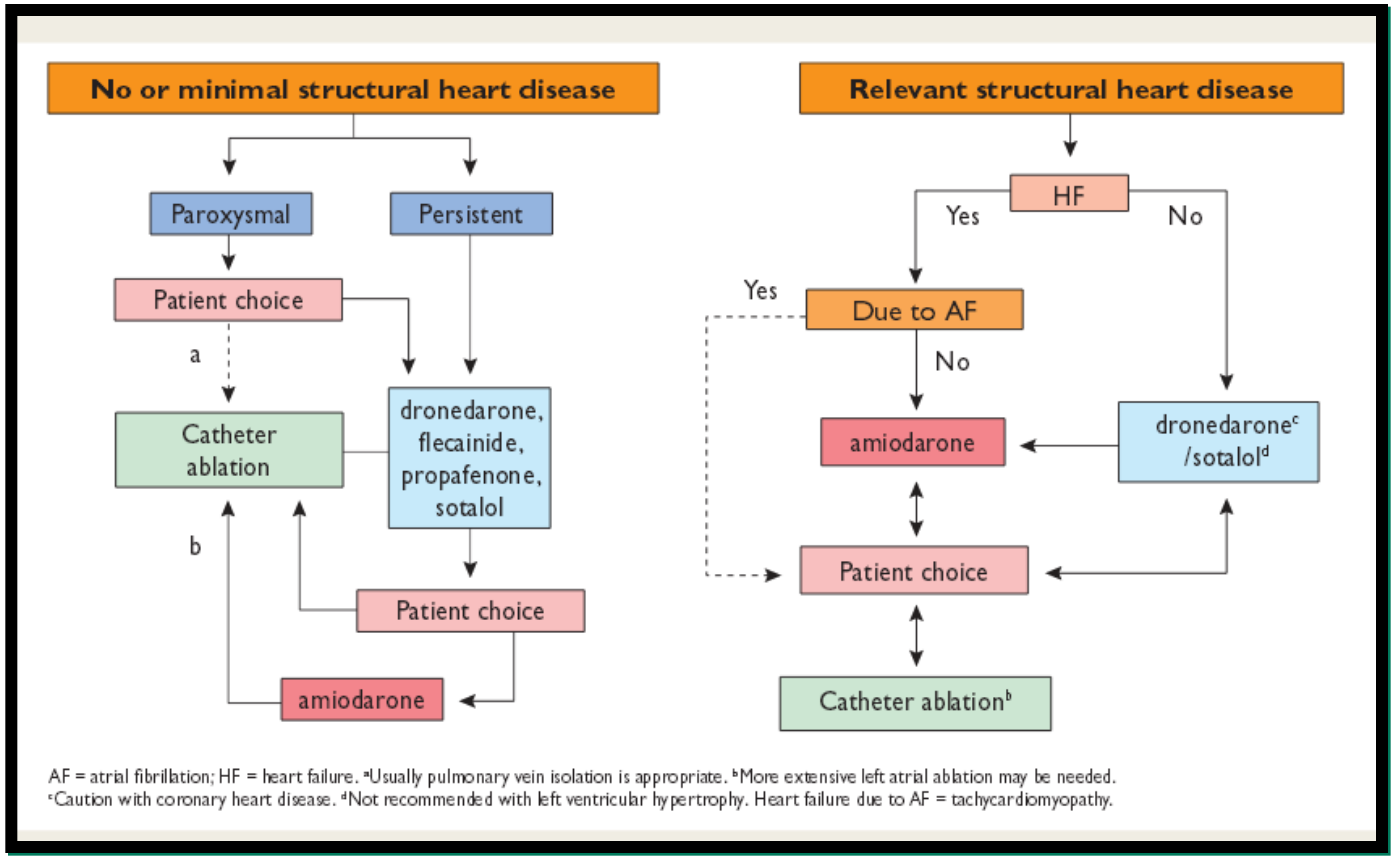
No. at Risk					
Rhythm control	593	514	378	228	82
Rate control	604	521	381	219	69

Roy D et al. *N Engl J Med* 2008; 358:2667-77

Non-Pharmacologic Rhythm Control



AF ablation guidelines



AF = atrial fibrillation; HF = heart failure. [a]Usually pulmonary vein isolation is appropriate. [b]More extensive left atrial ablation may be needed. [c]Caution with coronary heart disease. [d]Not recommended with left ventricular hypertrophy. Heart failure due to AF = tachycardiomyopathy.

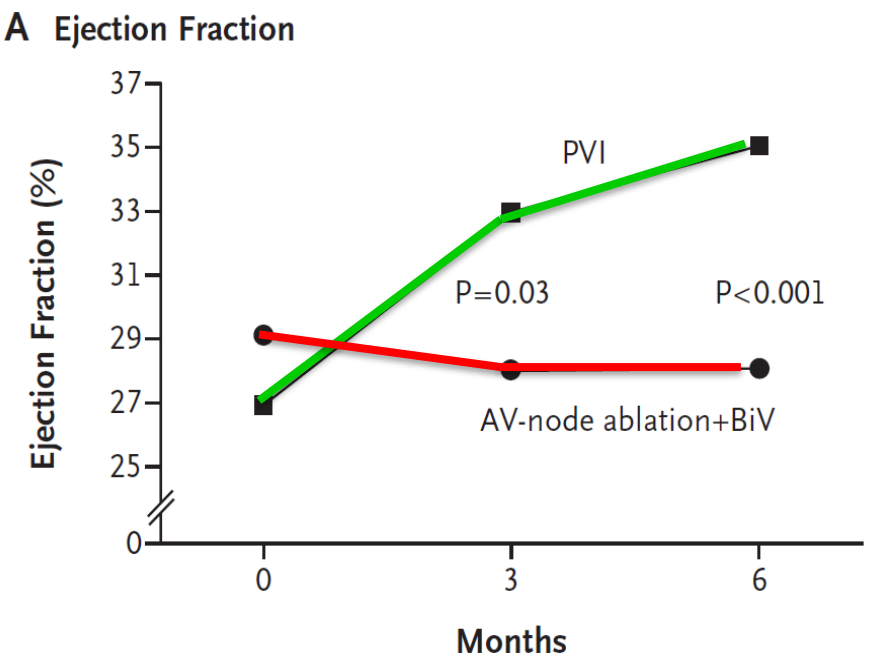
Recommendations	Class[a]	Level[b]
Catheter ablation of symptomatic paroxysmal AF is recommended in patients who have symptomatic recurrences of AF on antiarrhythmic drug therapy (amiodarone, dronedarone, flecainide, propafenone, sotalol) and who prefer further rhythm control therapy, when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced centre.	I	A
Catheter ablation of AF should target isolation of the pulmonary veins.	IIa	A
Catheter ablation of AF should be considered as first-line therapy in selected patients with symptomatic paroxysmal AF as an alternative to antiarrhythmic drug therapy, considering patient choice, benefit, and risk.	IIa	B
When catheter ablation of AF is planned, continuation of oral anticoagulation with a VKA should be considered during the procedure, maintaining an INR close to 2.0.	IIa	B
When AF recurs within the first 6 weeks after catheter ablation, a watch-and-wait rhythm control therapy should be considered.	IIa	B

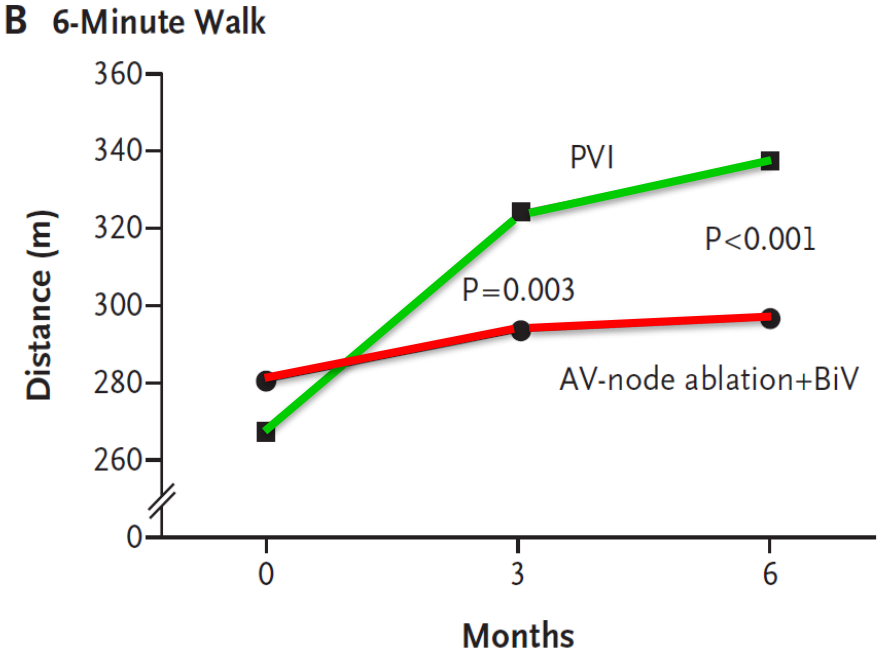
The NEW ENGLAND JOURNAL of MEDICINE

Pulmonary-Vein Isolation for Atrial Fibrillation in Patients with Heart Failure

EF improved in 76% of patients
Improvement in EF by 8±8%

Distance increase 71 m
Improvement by 26%





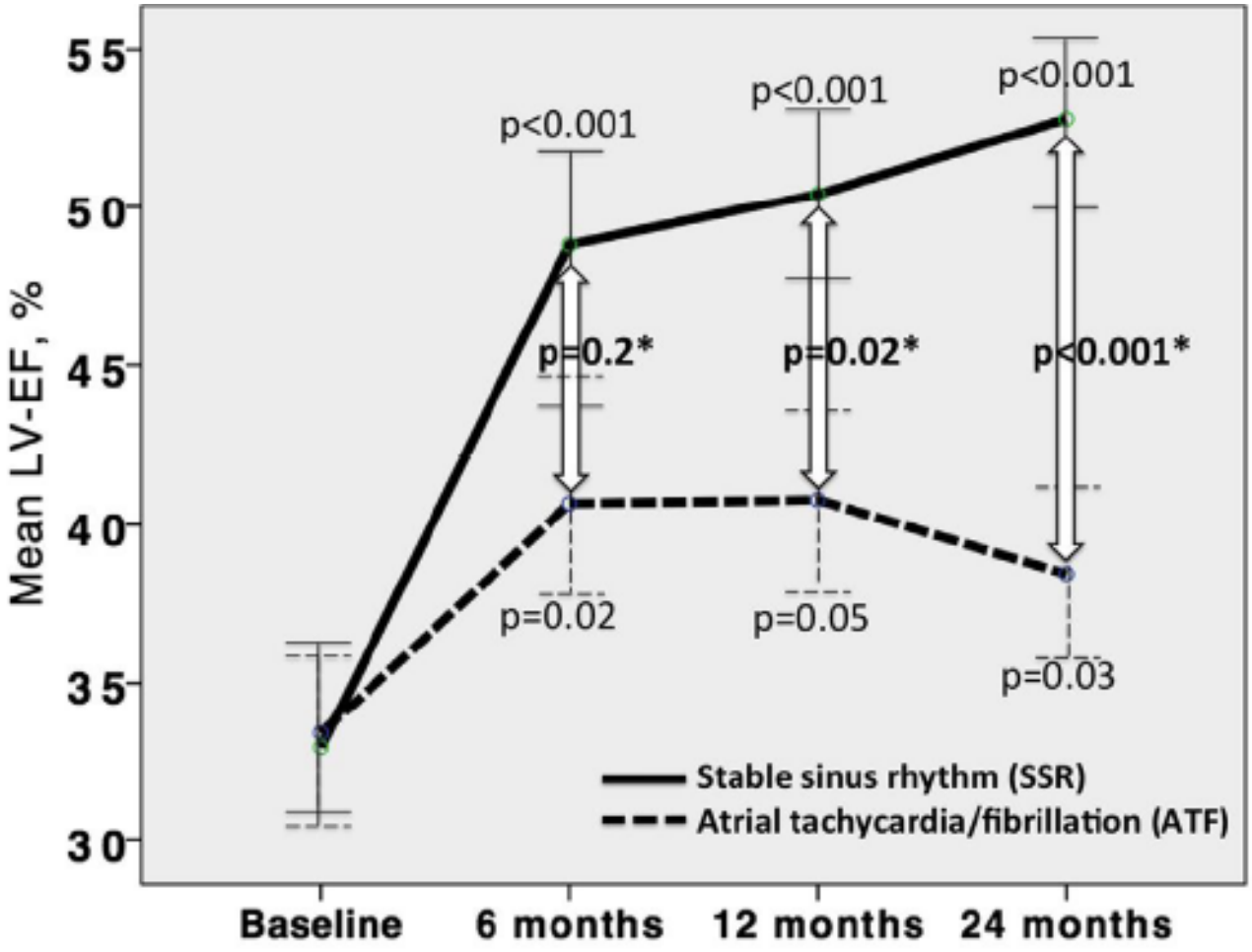
EF improved in 25% of pts
Decrease in EF by 1±4%

Distance increase 16 m
Improvement by 6%

Khan et al. *NEJM* 2008;359:1778-85

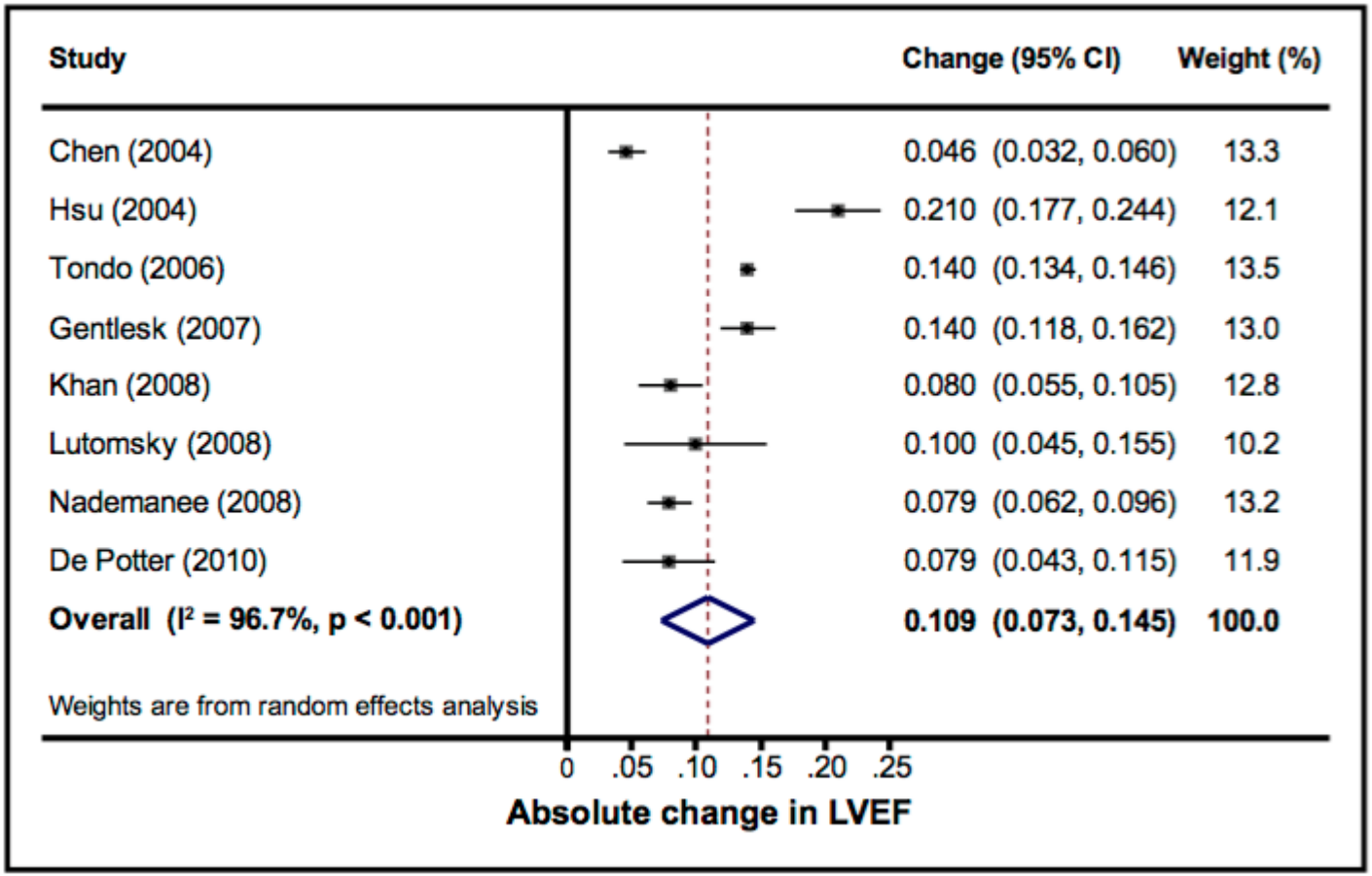
AF ablation in heart failure

Impact of follow-up heart rhythm on LVEF



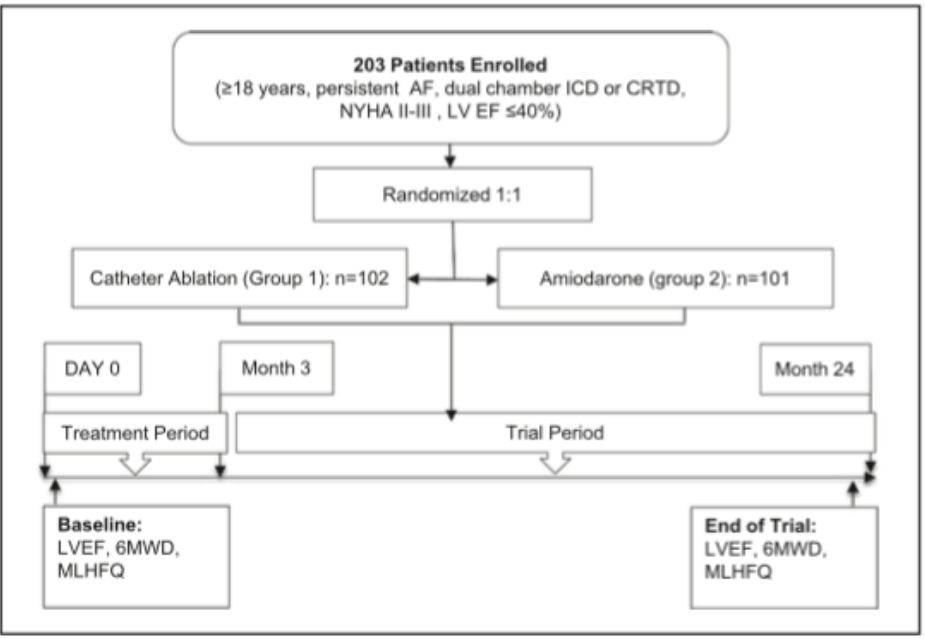
Nedios, Heart Rhythm 2014

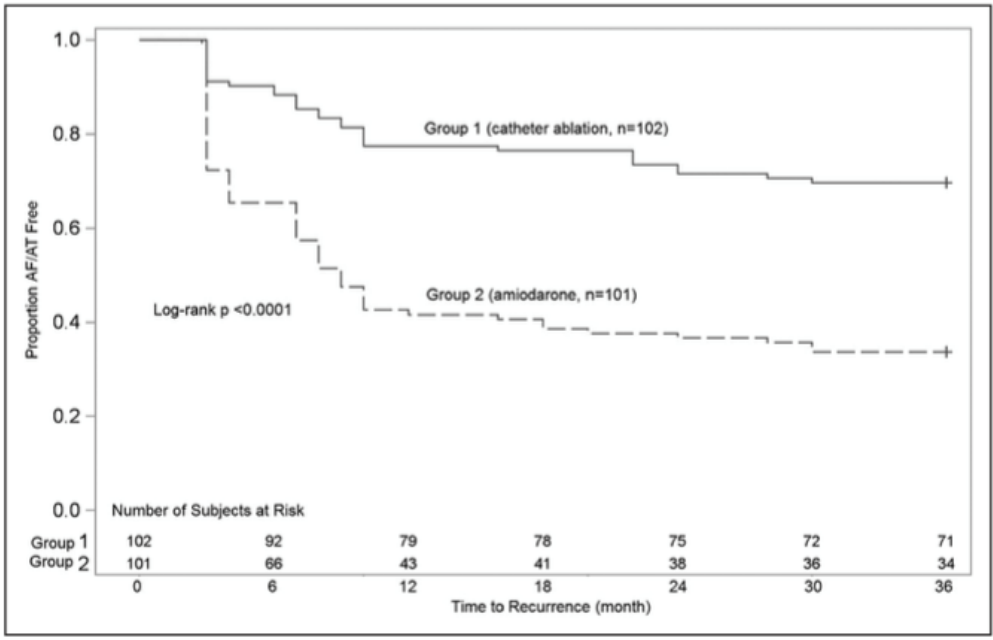
AF ablation improved LVEF in HF patients



Wilton SB, et al. Am J Cardiol 2010;106:1284–1291

AF ablation is better than drugs in HF patients





Di Biase L, et al. Circulation. 2016;133:1637-1644

AF Ablation in Pts with LV Systolic Dysfunction Long-term outcomes

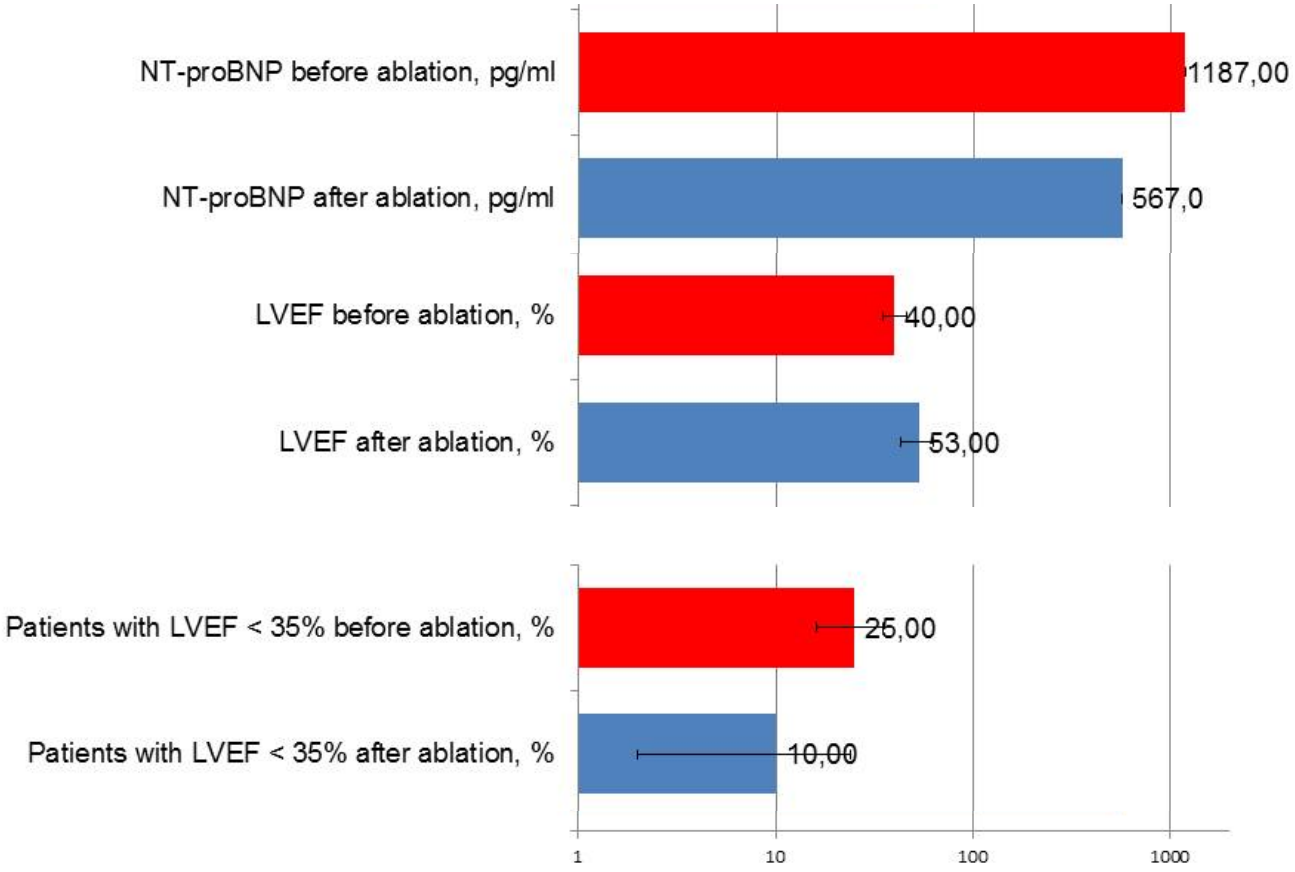
Catheter Ablation of Atrial Fibrillation in Patients with Left Ventricular Systolic Dysfunction: A Systematic Review and Meta-analysis

Matteo Anselmino, Mario Matta, Fabrizio D'Ascenzo, Thomas J. Bunch, Richard J. Schilling, Ross J. Hunter, Carlo Pappone, Thomas Neumann, Georg Nolker, Martin Fiala, Emanuele Bertaglia, Antonio Frontera, Edward Duncan, Stuart Thomas, Pierre Jais, Rukshen Weerasooriya, Jon M. Kalman, Fiorenzo Gaita. *Circ Arrhythm Electrophysiol* 2014

Multicenter individual patient data meta-analysis

- direct contact with each center with published long-term data
- **25 studies** included, **1838 patients**

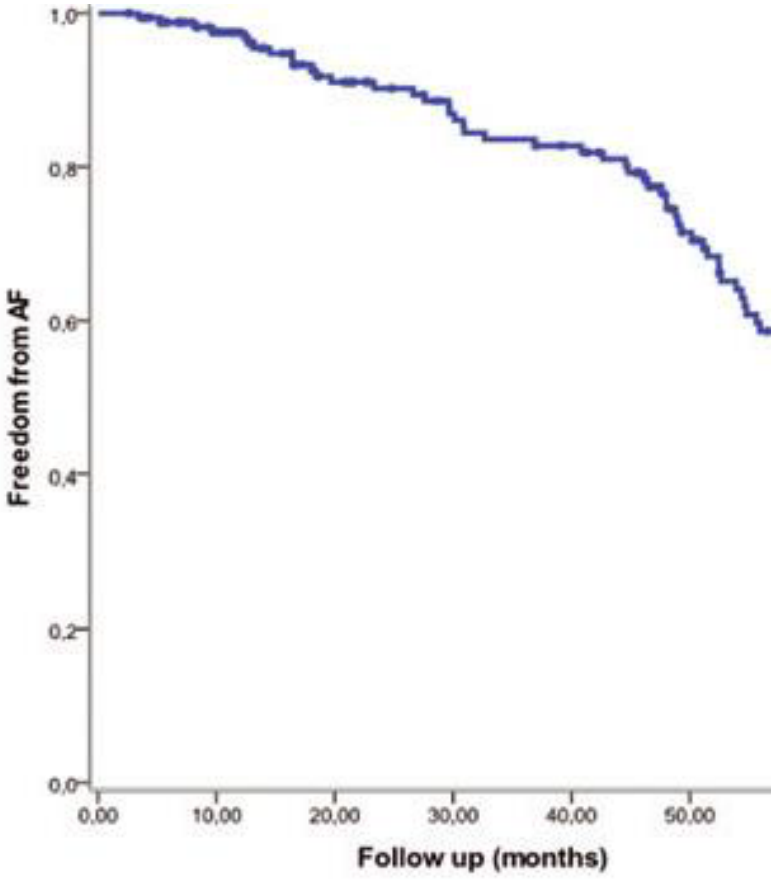
AF Ablation in Pts with LV Systolic Dysfunction
Impact on Left Ventricular Function



Anselmino M, Gaita F et al *Circ Arrhythm Electrophysiol* 2014

Long-Term Results of Transcatheter Atrial Fibrillation Ablation in Patients with Impaired Left Ventricular Systolic Function

MATTEO ANSELMINO, M.D., PH.D.,* STEFANO GROSSI, M.D.,† MARCO SCAGLIONE, M.D.,‡
DAVIDE CASTAGNO, M.D.,* FRANCESCA BIANCHI, M.D.,† GAETANO SENATORE, M.D.,§
MARIO MATTA, M.D.,* DARIO CASOLATI, M.D.,* FEDERICO FERRARIS, M.D.,*
YVONNE CRISTOFORETTI, M.D.,* ALESSANDRO NEGRO, M.D.,*
and FIORENZO GAITA, M.D.*



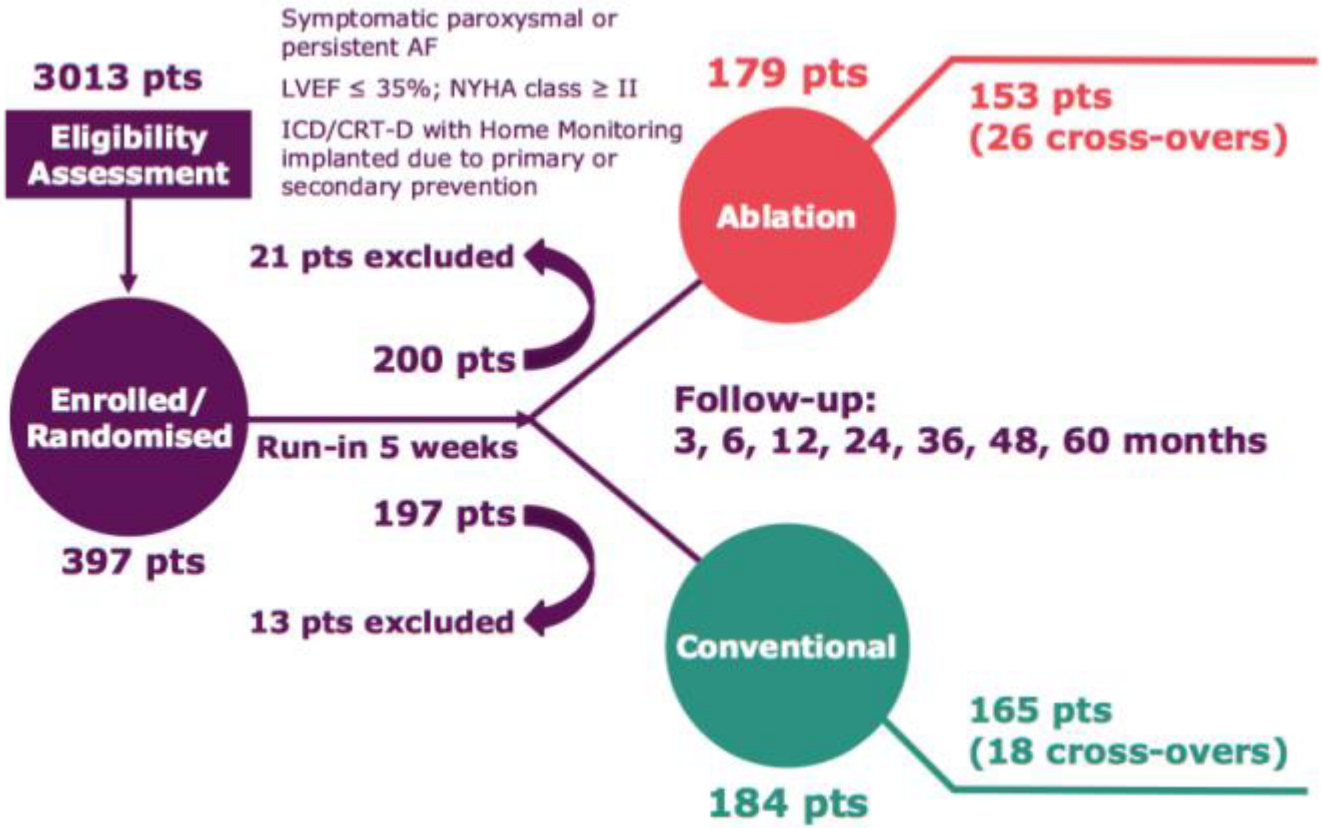
196 patients,
46 months mean follow-up
78% pers AF, 22% parox AF
15% PVI, 85%
PVI+lines/CFAE
62% patients free from AF

J CardiovascElectrophysiol 2013

Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*

NEJM 2018



Primary Endpoint

All-cause mortality + Worsening heart failure admissions

N. Marrouche (Salt Lake City, USA) 1.

Catheter Ablation for Atrial Fibrillation with Heart Failure

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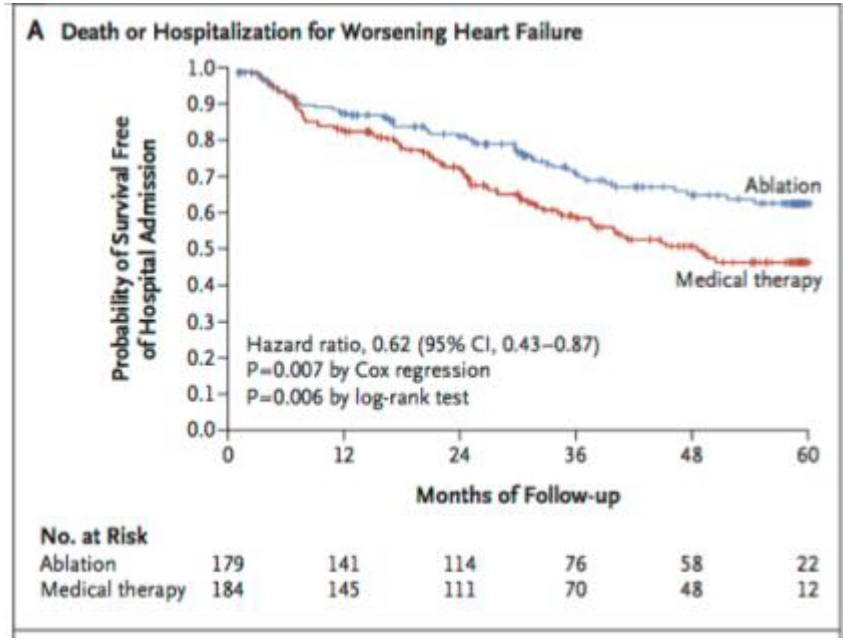

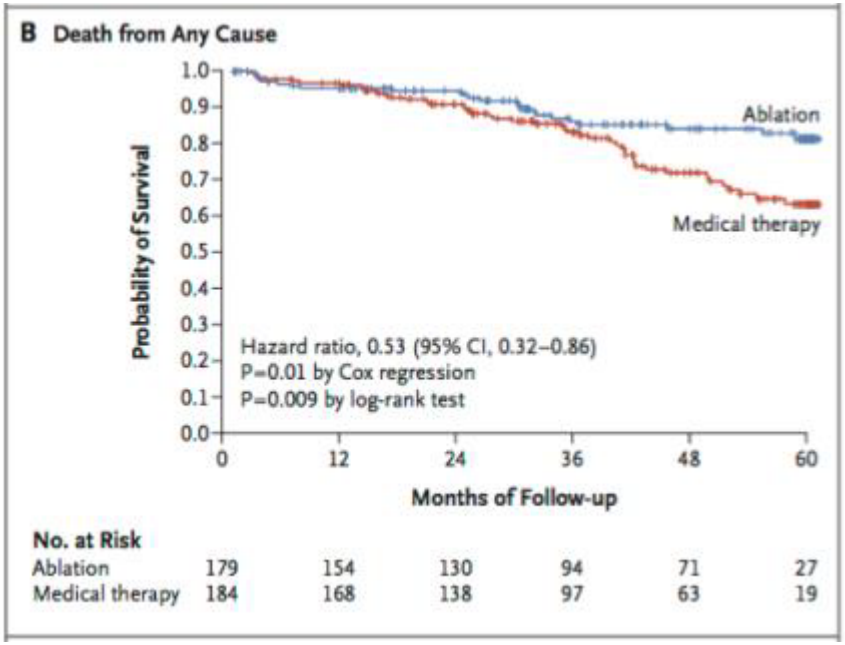

Marrouche NF, et al. N Engl J Med 2018;378:417-27

Take Home Messages

In the era of worldwide population ageing we are facing two growing epidemics (i.e. AF and HF) impacting on QoL, prognosis and costs

Rhythm control (especially TC ablation) is underused in patients with HF and AF

The key to success is an early treatment in selected patients which may provide significant symptomatic and prognostic benefit