

CONGRESS CENTRE, INSTITUTE FOR CLINICAL  
AND EXPERIMENTAL MEDICINE (IKEM), PRAGUE  
JUNE 12, 2019

20 years

of cardiac  
resynchronization therapy  
in the Czech Republic



[www.kardio-cz.cz](http://www.kardio-cz.cz)



Lékařská  
fakulta

Univerzita Palackého  
v Olomouci



# Role of catheter ablations in patients with heart failure

Tomáš Skála

# AF and HF – pathophysiology

**AF in HF** → 10–57% (dep. on HF severity)

**HF in AF** (persistent/long-standing persistent) → 40-55%

*Santhanakrishnan R. Circulation 2016*

**Increased risk of mortality synergistically** confer worse outcomes compared with either condition alone

↑ *rates of stroke, HF hospitalization, and death*

*Mamas MA, Eur J Heart Fail 2009*

## **AF → HF**

loss of atrial contraction to ventricular filling - ↓ diastolic function and ↓ CO by up to 25%

uncontrolled rapid ventricular conduction - impaired myocardial contractility - LV systolic dysfunction - tachycardia-induced CMP

irregular ventricular conduction - itself ↓CO

*Nerheim P, Circulation 2004*

## **HF → AF**

ventricular dysfunction → atrial structural and electrical changes by several hemodynamic, mechanical, and neurohormonal mechanisms → atrial stretch and fibrosis → AF

*Li D, Circulation 2001*

***...vicious electromechanical cycle between AF and HF...***

# AF and HF – what to do?

## Drugs:

1. *Rhythm control* – pharmacological
2. Permanent AF, pharmacological *rate-control*

## Devices and interventions (non-pharmacological):

3. *Rhythm control* – complex *catheter ablation*
4. Permanent AF, *pace and ablate*

# Rate vs. pharmacological rhythm control (general population)

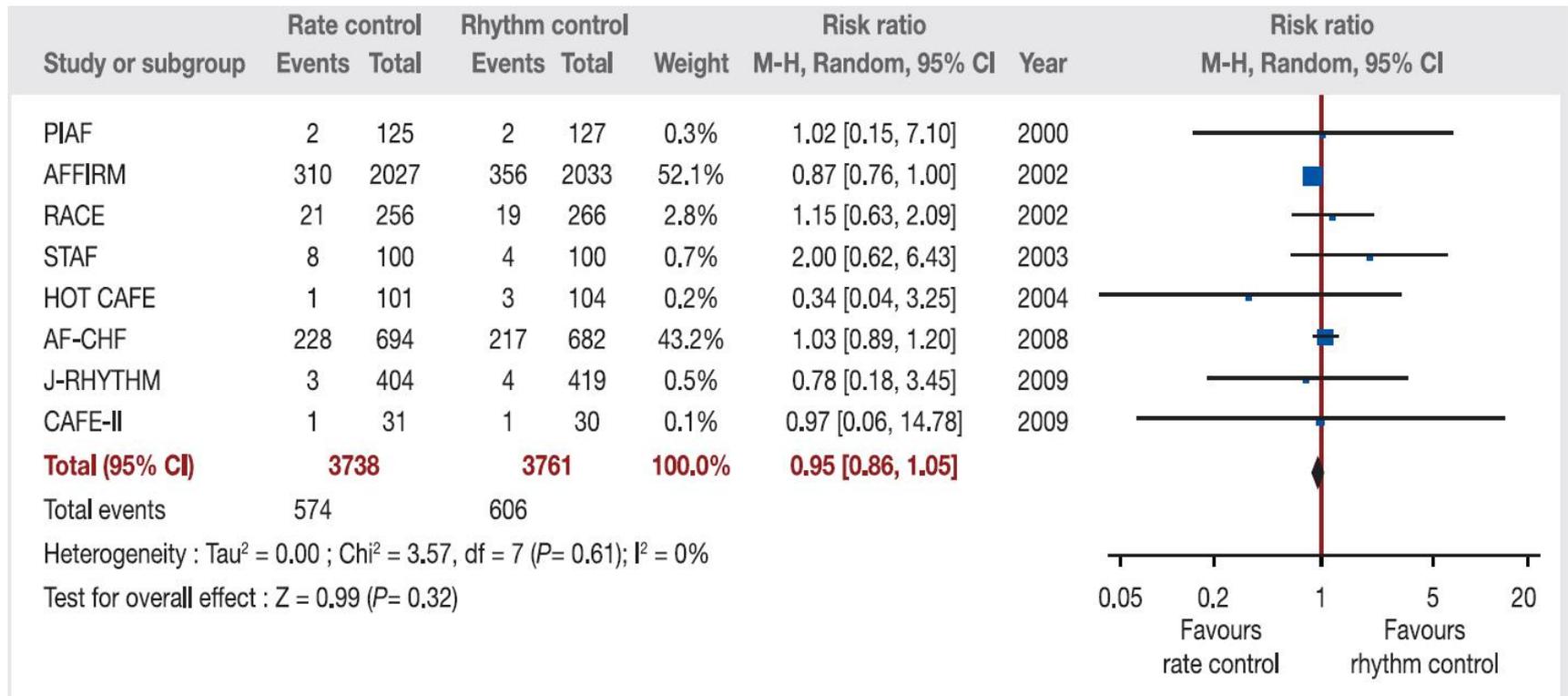
8 RCTs (7,499 patients)

no significant differences in

**all-cause mortality** (RR: 0.95; CI: 0.86–1.05)

**CV mortality** (RR: 0.99; CI: 0.87–1.13)

**sudden death** (RR:1.12; CI: 0.91–1.38)



Rhythm Control versus Rate Control  
for Atrial Fibrillation and Heart Failure

Denis Roy, M.D., Mario Talajic, M.D., Stanley Nattel, M.D., D. George Wyse, M.D., Ph.D., Paul Dorian, M.D.,  
Kerry L. Lee, Ph.D., Marital G. Bourassa, M.D., Malcolm O. Arnold, M.D., Alfred E. Buxton, M.D.,  
A. John Camm, M.D., Stuart J. Connolly, M.D., Marc Dubuc, M.D., Anique Ducharme, M.D., M.Sc.,  
Peter G. Guerra, M.D., Stefan H. Hohnloser, M.D., Jean Lambert, Ph.D., Jean-Yves Le Heuzey, M.D.,  
Gilles O'Hara, M.D., Ole Dyg Pedersen, M.D., Jean-Lucien Rouleau, M.D., Bramah N. Singh, M.D., D.Sc.,  
Lynne Warner Stevenson, M.D., William G. Stevenson, M.D., Bernard Thibault, M.D., and Albert L. Waldo, M.D.,  
for the Atrial Fibrillation and Congestive Heart Failure Investigators\*

# Rate vs. pharmacological rhythm control (heart failure patients)

## AF-CHF study

1,376 patients

AF (33% paroxysmal, 67% persistent)

NYHA II-IV

LVEF < 35%

**pharmacologic rhythm control (mostly amiodarone) vs. pharmacologic rate control**

FU 47 months, SR:

**pharmacologic rhythm control**                      73%

**rate control**    35%

# Rate vs. pharmacological rhythm control

## AF-CHF study

### no difference in:

**cardiovascular mortality**

(HR 1.06, 95% CI 0.86–1.30; P = 0.59)

**worsening HF**

(HR 0.87, 95% CI 0.72–1.06, P = 0.17)

**all-cause mortality**

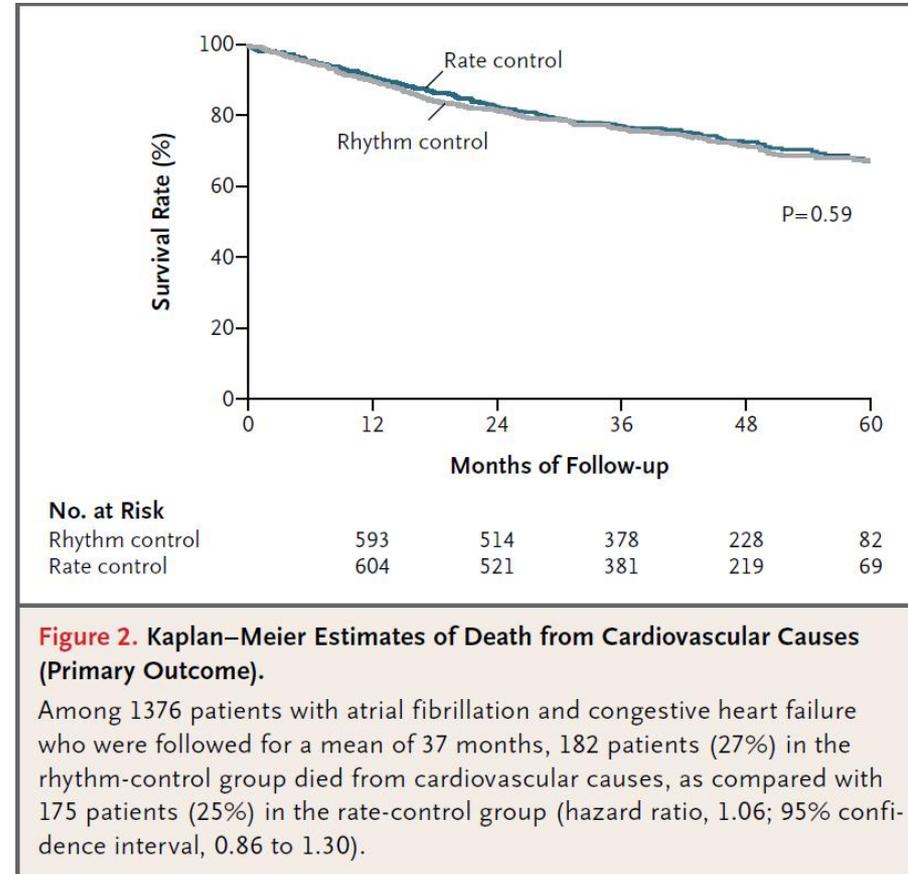
(HR 0.97, 95% CI 0.80–1.17, P = 0.73)

(similar to the AFFIRM trial)

## **amiodarone**

associated with a high discontinuation rate and its use

is suggested to be associated with  $\uparrow$  non-CV death



Steinberg JS, Circulation, 2004

In some HF patients, we can achieve SR with amiodarone.

But compared with patients left on rate-control, we will not lower their mortality.

# Non-pharmacological rhythm-control

Trial (year of publication)	N	Inclusion criteria	Treatment arms	Primary endpoint	FU (months)	Main observations
PABA-CHF (2008) <sup>56</sup>	81	Paroxysmal or persistent AF, NYHA II-III, and LVEF ≤40%	PVI (± additional ablation) vs. CRT plus AV node ablation	Composite of LVEF (echo), 6MWD or MLWHF score	6	88% AF-free survival in ablation arm (71% off AAD); significant increase in LVEF (+8 vs. -1%), functional capacity, and QOL
MacDonald <i>et al.</i> (2011) <sup>57</sup>	41	Persistent AF, NYHA II-IV, and LVEF <35%	PVI (± additional ablation) vs. pharmacological rate control	Change in LVEF (MRI)	6	50% AF-free survival in ablation arm (50% off AAD); non-significant increase in LVEF (significant if sinus rhythm: +10 vs. +1%), functional capacity, and QOL
ARC-HF (2013) <sup>58</sup>	52	Persistent AF, NYHA II-IV, and LVEF ≤35%	PVI (± additional ablation) vs. pharmacological rate control	Change in peak oxygen consumption	12	88% AF-free survival in ablation arm (84% off AAD); significant improvement in peak VO <sub>2</sub> , QOL, and BNP; non-significant increase in LVEF (+11 vs. +5%) and 6MWD
CAMTAF (2014) <sup>59</sup>	50	Persistent AF, NYHA II-IV, and LVEF <50%	PVI (± additional ablation) vs. pharmacological rate control	Change in LVEF (echo)	6	81% AF-free survival in ablation arm (81% off AAD); significant improvement in LVEF (+8 vs. -3%), functional capacity, QOL, and BNP
AATAC-AF (2016) <sup>60</sup>	203	Persistent AF, NYHA II-III, LVEF ≤40%, and DC-ICD/CRT-D	PVI (± additional ablation) vs. amiodarone	AF-free survival	24	70% AF-free survival in ablation arm (on/off AAD) vs. 34% in amiodarone arm; significant improvement in LVEF (+8 vs. +6%), mortality (8 vs. 18%), hospitalization (31 vs. 57%), and QOL
CAMERA-MRI (2017) <sup>33</sup>	68	Persistent AF, NYHA II-IV, LVEF ≤45%, and idiopathic cardiomyopathy <sup>a</sup>	PVI + posterior box isolation vs. pharmacological rate control	Change in LVEF (MRI)	6	75% AF-free survival in ablation arm (56% off AAD); significant improvement in LVEF (+18 vs. +4%) and LVEF normalization ≥50% (58 vs. 9%); LGE - predicted LVEF improvement and normalization
CASTLE-AF (2018) <sup>61</sup>	363	Paroxysmal or persistent AF, NYHA II-IV, LVEF ≤35%, and DC-ICD/CRT-D with remote monitoring	PVI (± additional ablation) vs. pharmacological rate (70%) or rhythm control (30%)	Composite of HF hospitalization or all-cause mortality	60 (median 38)	63 vs. 22% maintained SR at 5 years; significant improvement in LVEF (+8 vs. 0%), all-cause mortality or HF hospitalization (28 vs. 44%), all-cause mortality (13 vs. 25%), cardiovascular mortality (11 vs. 22%), and HF hospitalization (21 vs. 36%)

### A Randomized Trial to Assess Catheter Ablation Versus Rate Control in the Management of Persistent Atrial Fibrillation in Heart Failure

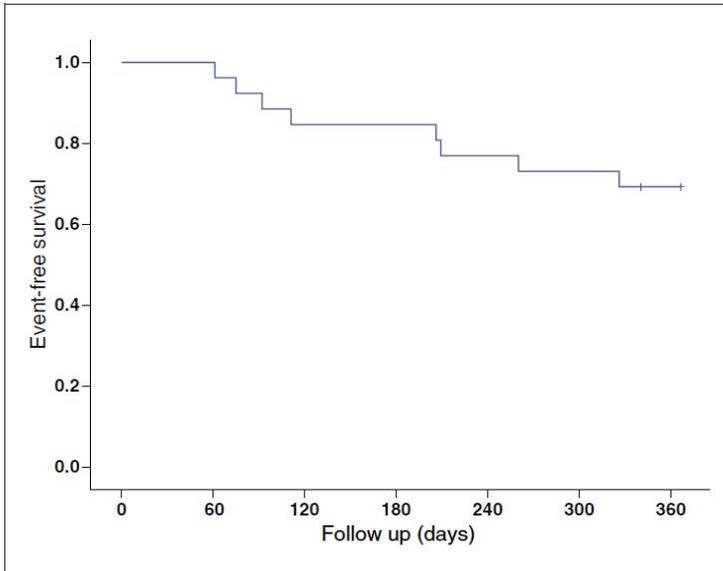
David G. Jones, MD,\*† Shouvik K. Halder, MBBS,\*† Wajid Hussain, MB, ChB,\*† Rakesh Sharma, PhD,\*† Darrel P. Francis, MD,† Shelley L. Rahman-Haley, MD,\*† Theresa A. McDonough, MD,\*† S. Richard Underwood, MD,\*† Vias Markides, MD,\*† Tom Wong, MD\*†  
London, United Kingdom

# Non-pharmacological rhythm-control

## ARC-CHF

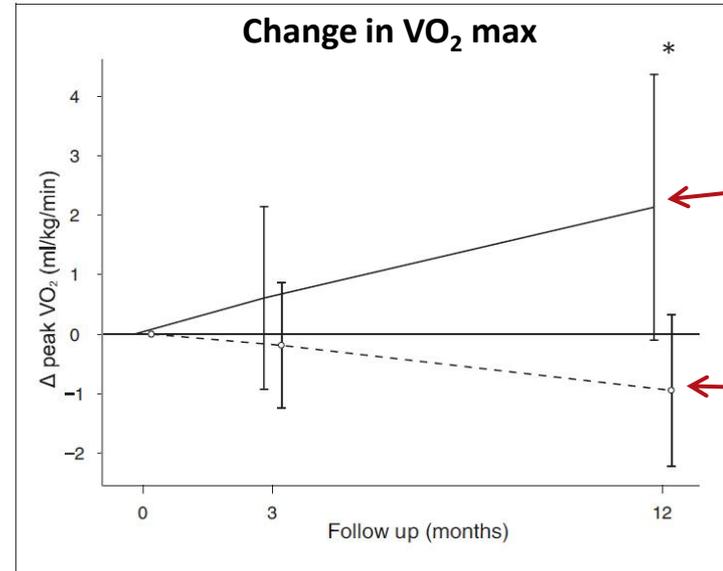
## AF ablation vs. pharmacological rate control

persistent AF, LV dysfunction



**Figure 6** Single Procedure Atrial Arrhythmia-Free Survival at 1 Year

Intention-to-treat Kaplan-Meier atrial arrhythmia-free survival estimation after a single ablation procedure. The blanking period was set at 2 months, after which occurrence of documented atrial tachyarrhythmia constituted procedural failure.



**Figure 2** Primary Endpoint: Summary Data

By intention-to-treat, change (Δ) in peak oxygen consumption (VO<sub>2</sub>) (mean ± 95% confidence interval) from baseline, comparing ablation (solid dot/line) versus rate control (open dot and dashed line) at 3- (p = 0.38) and 12-month (p = 0.018) follow-up. Statistical significance shown between groups at each time point: \*if p < 0.05.

Ablation

Rate-control

# Non-pharmacological rhythm-control

## CAMTAF

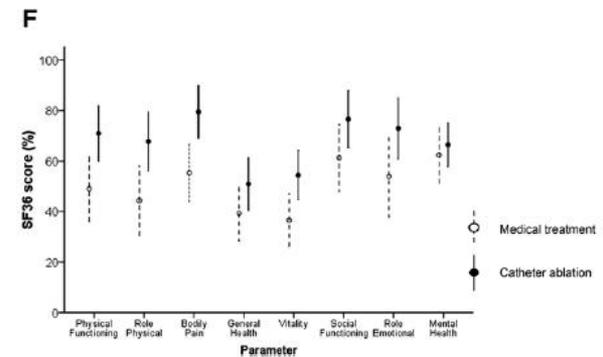
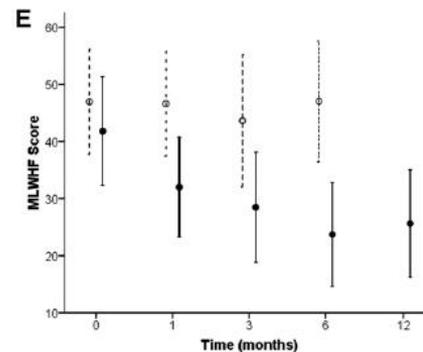
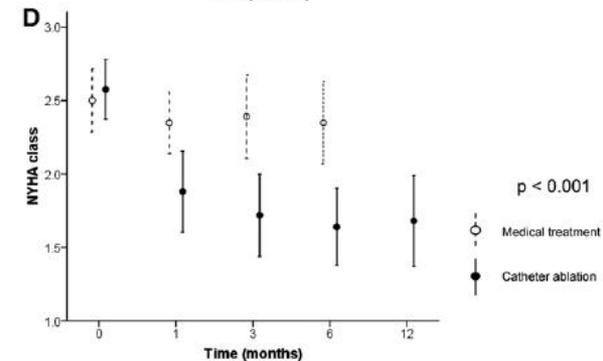
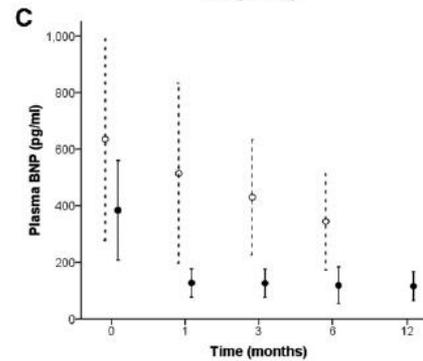
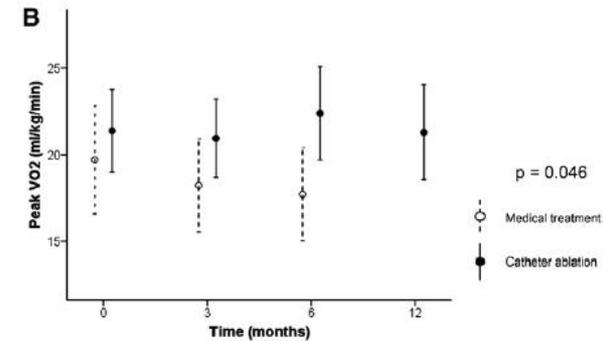
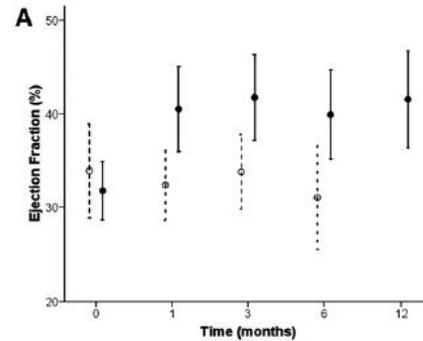
AF ablation

vs.

pharmacological rate control

persistent Af, LV dysfunction

↑ LVEF (+8% vs. -3%;  $P < 0.001$ )



**...Ablation is better than rate-control in improvement of objective signs of HF...**

# Non-pharmacological rhythm-control

## AATAC-AF

### AF ablation vs. amiodarone

203 patients

persistent AF

NYHA II–III

LVEF <40%

FU 2 years, (1.4± 0.6 procedures)

### Arrhythmia-free:

**AF ablation** 70%

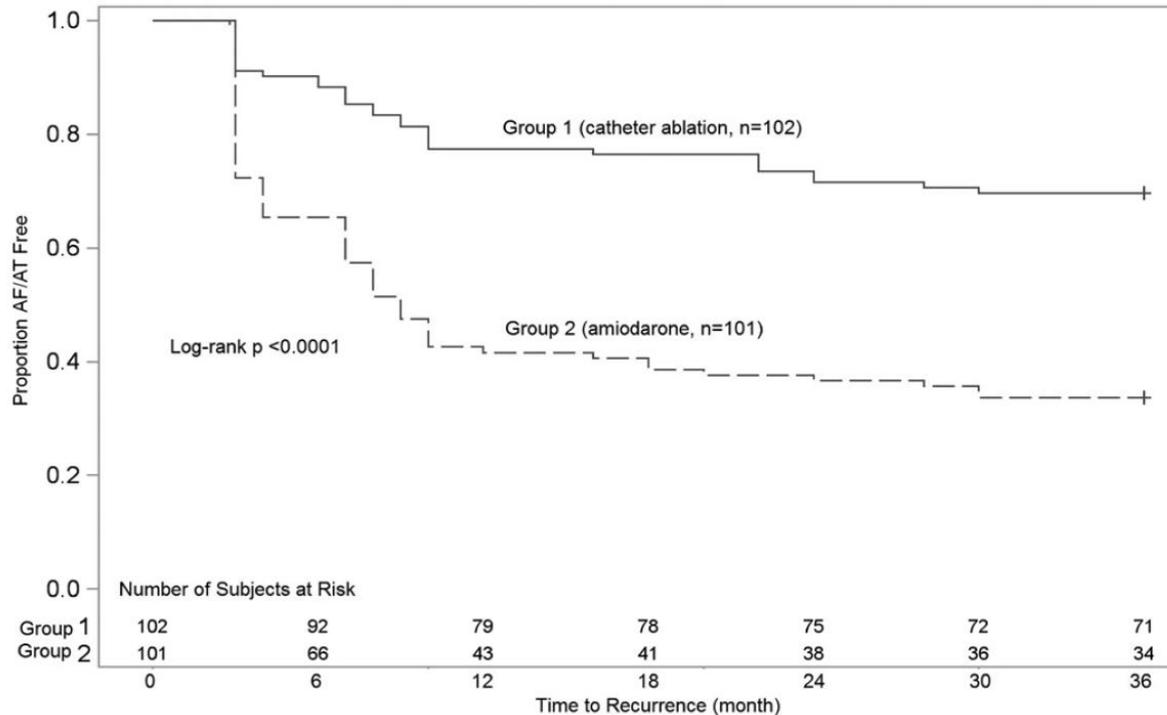
**amiodarone** 34%

### Mortality:

**AF ablation** 8%

**amiodarone** 18 %

(P=0.037)



**...ablation is superior to amiodarone in maintaining of SR and in lowering of mortality rate...**

# Non-pharmacological rhythm-control

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., Herbert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators\*

## CASTLE-AF

### AF ablation vs. medication (rate or rhythm control)

rate-control 70%, amiodarone 30%

### primary end-point: all-cause mortality and hospitalization for worsening HF

363 patients; paroxysmal or persistent AF

NYHA II–IV; LVEF <35%

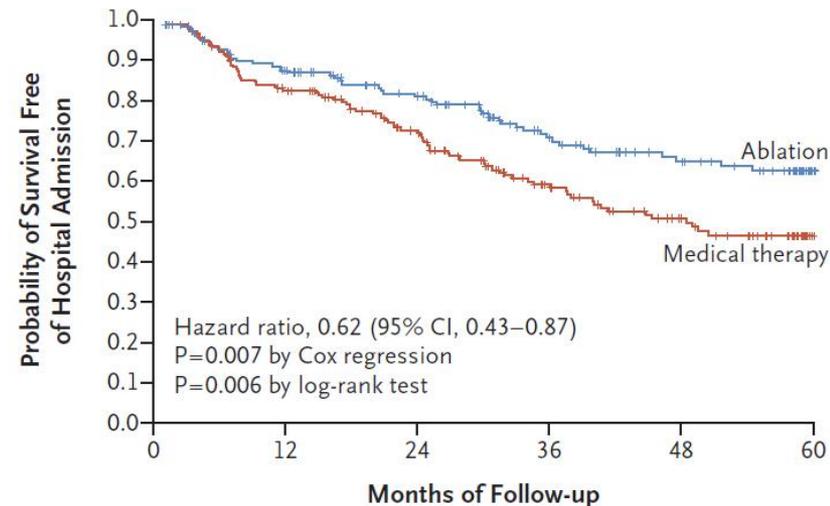
FU 5 years

death from any cause (13.4% vs. 25.0%)

heart failure hospitalization (20.7% vs. 35.9%)

NNT 8.3 patients to prevent one primary outcome event

Death or Hospitalization for Worsening Heart Failure



#### No. at Risk

Ablation	179	141	114	76	58	22
Medical therapy	184	145	111	70	48	12

**...AF ablation is better than any medication (rate or rhythm control) in lowering of mortality rate...**

# Non-pharmacological rhythm-control

## 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., Herbert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators\*

### CASTLE-AF

#### ablation-based rhythm control vs. medication

(rate-control 70% or amiodarone 30%)

SR in 63% of cases at 5 years

catheter ablation ↓ AF burden ...

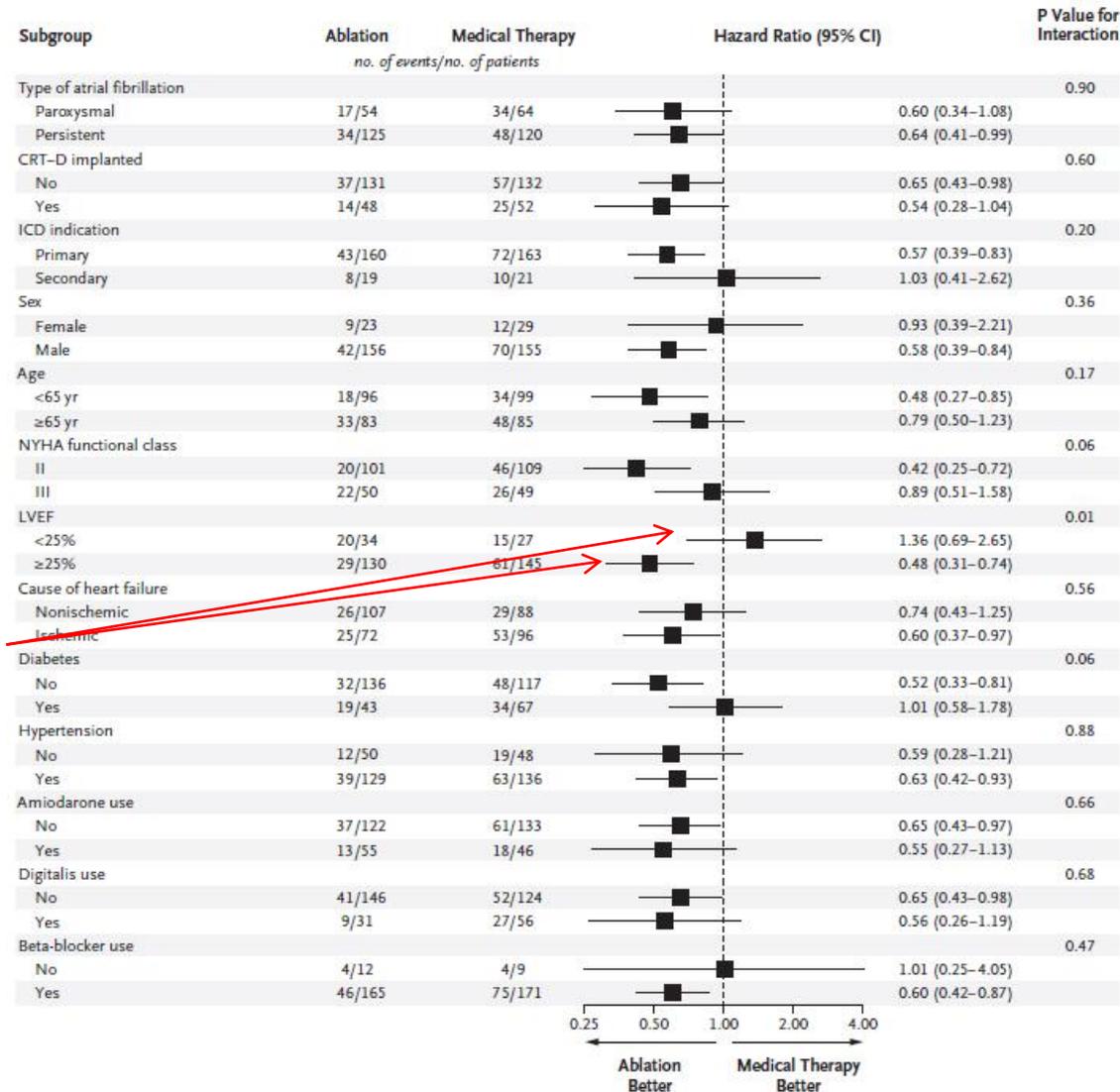
Ablation: AF burden 27%

Medical th: AF burden 64%

LVEF >25% more likely to benefit from AF ablation

68% of patients in the ablation group ↑LVEF

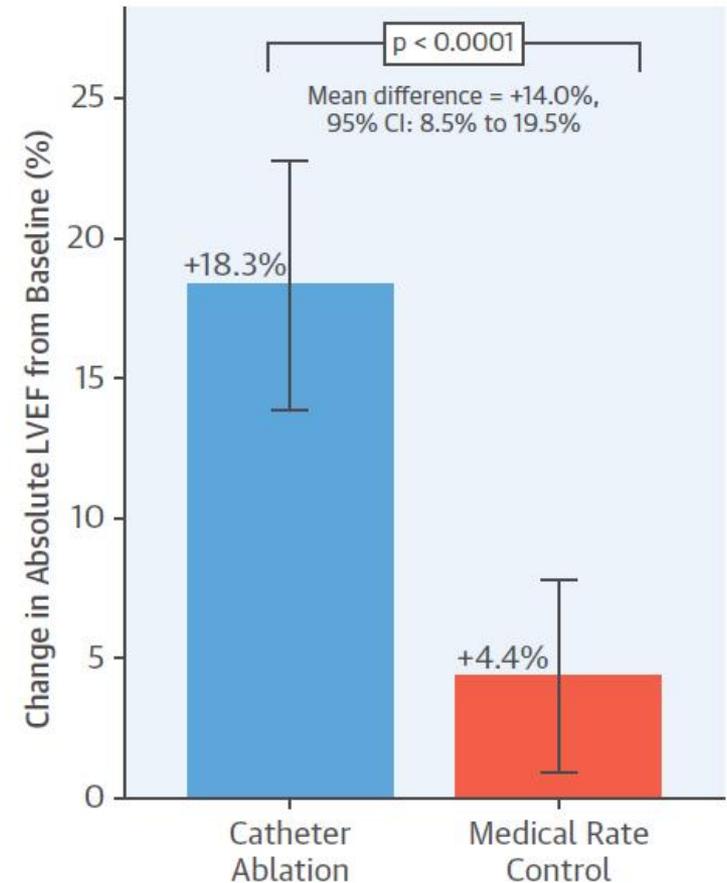
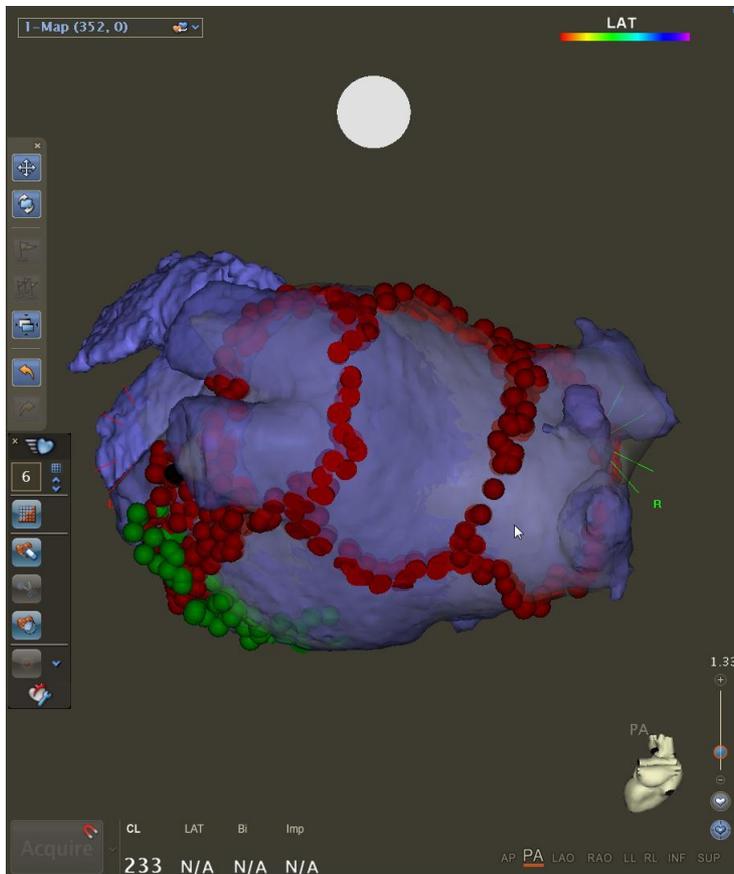
beyond the magical cut-off of 35%...



# Non-pharmacological rhythm-control

## CAMERA-MRI

### AF ablation vs. pharmacological rate control



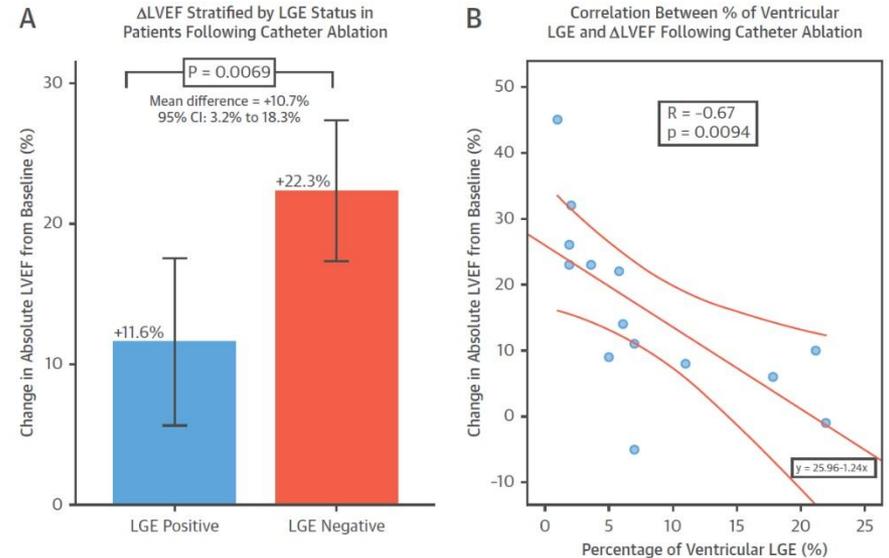
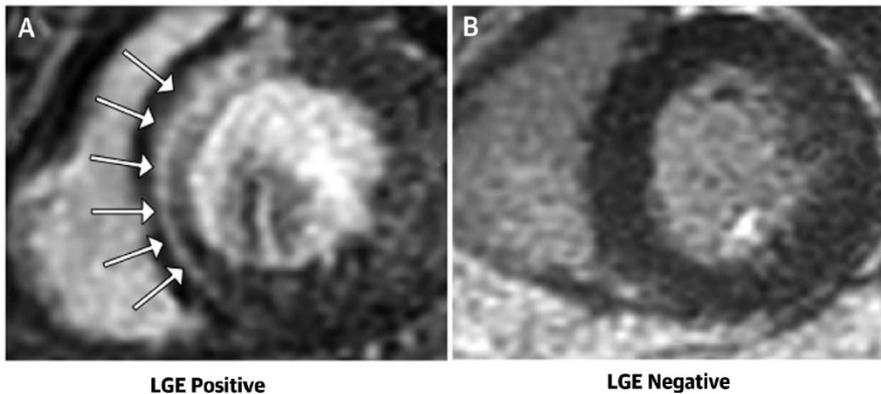
# Non-pharmacological rhythm-control

## CAMERA-MRI

### AF ablation vs. pharmacological rate control

↑ LVEF after AF ablation in patients without LE in LV

Late gadolinium enhancement demonstrating regional midwall fibrosis in dilated cardiomyopathy



...we can select patients in whom AF ablation will most likely be more beneficial than in others...

# Non-pharmacological rate-control ....pace and ablate

2011/2012 US National Cardiovascular Data

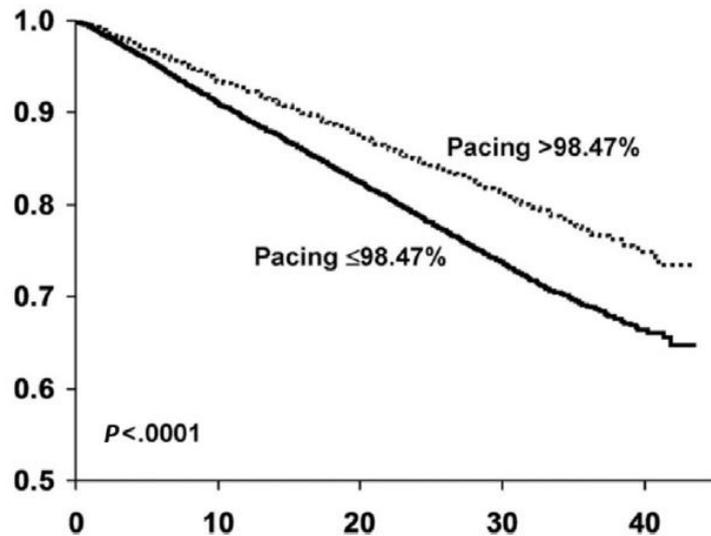
**36%** of 87,692 **CRT-D - AF**

**31%** of 326,000 **ICD - AF**

NCDR ICD Registry 2011-2 Data

36,000 patients, 2 years FU

pacing > **98.5%** much better outcomes



To maximize clinical response to CRT, pacing must be delivered nearly universally

# Pace and ablate

## RAFT study

1798 patients

12.7% (229) permanent AF, with:

HR <60 bpm at rest

HR <90 bpm after 6MHW

randomized to **CRT-D** vs. **ICD**

Primary endpoint: **HF hospitalization or death**

...**no difference** in outcomes between the 2 groups

*only 34% had greater than 95% pacing*

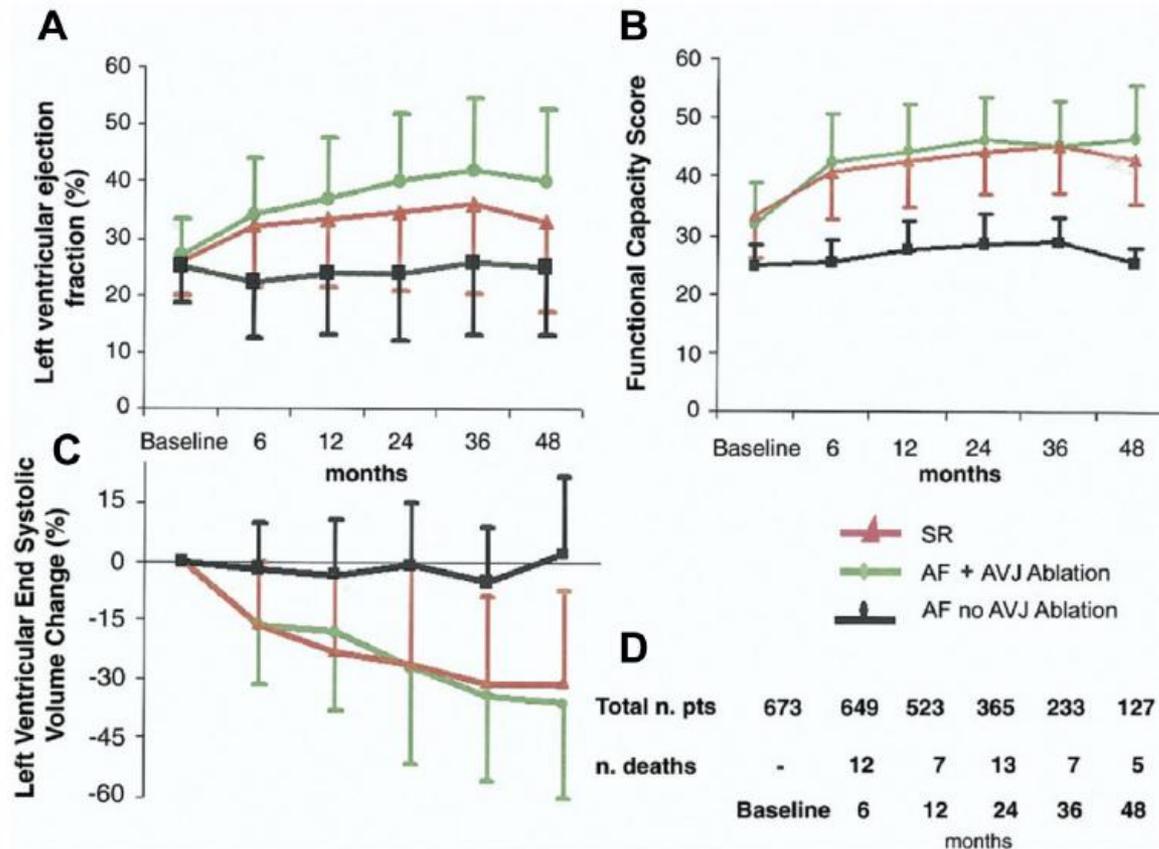
**...there are very limited data for the benefit of CRT in permanent AF (without AVN ablation)...**

# Pace and ablate

114 patients with CRT and AF - 42% achieved “adequate” biventricular capture (>85%)

Only the patients who had undergone **AVN ablation = reverse remodeling**

( $\uparrow$ LVEF,  $\downarrow$ LVESV) and functional improvement



# Pace and ablate

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

Maurizio Gasparini<sup>1\*</sup>, Angelo Auricchio<sup>2,3</sup>, Marco Metra<sup>4</sup>, François Regoli<sup>1</sup>, Cecilia Fantoni<sup>2,3</sup>, Barbara Lamp<sup>5</sup>, Antonio Curnis<sup>4</sup>, Juergen Vogt<sup>6</sup>, and Catherine Klersy<sup>6</sup> for the Multicentre Longitudinal Observational Study (MILOS) Group

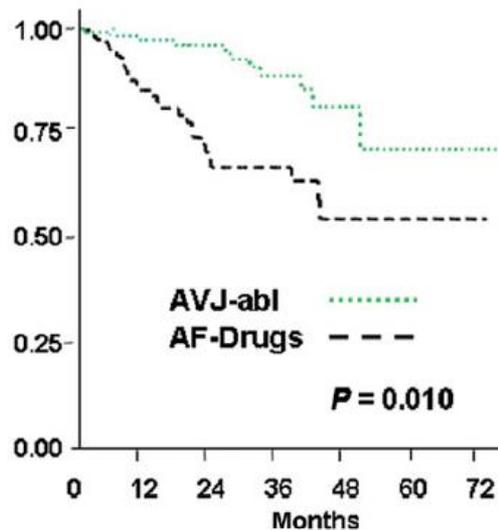
Mortality ↓ in AVN ablation, 4% versus 15% in pharm. rate-control.

AVN ablation in CRT ↓ mortality by 40 %

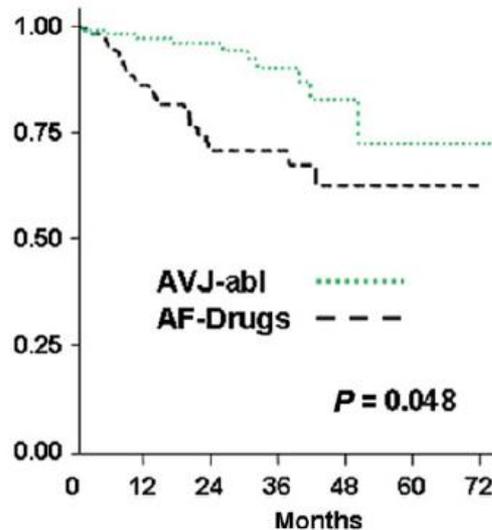
Wilton SB, Heart Rhythm 2011

Ganesan AN. J Am Coll Cardiol 2011

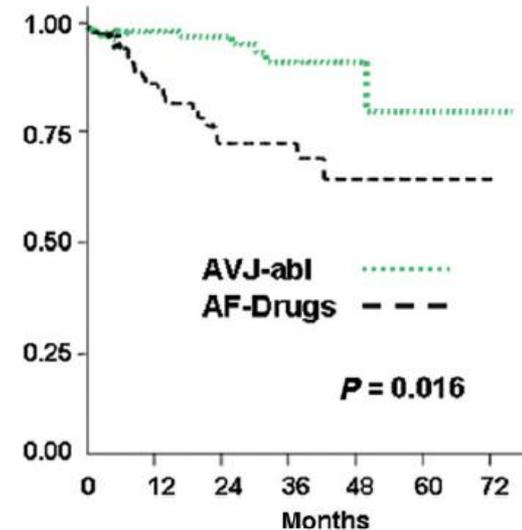
(A) AF Patients: Overall Survival



(B) AF Patients: Cardiac Survival



(C) AF Patients: HF Survival



...CRT? – AF? – not suitable for a complex AF ablation? – consider AVN ablation!...

# Pace and ablate

## APAF-CRT

### narrow QRS complex

### Optimal medical therapy vs. AVN ablation in CRT/permanent AF

hospitalized for HF in last 12 months

Any LVEF (42% <35%)

primary endpoint :

all-cause mortality + hospitalization for HF

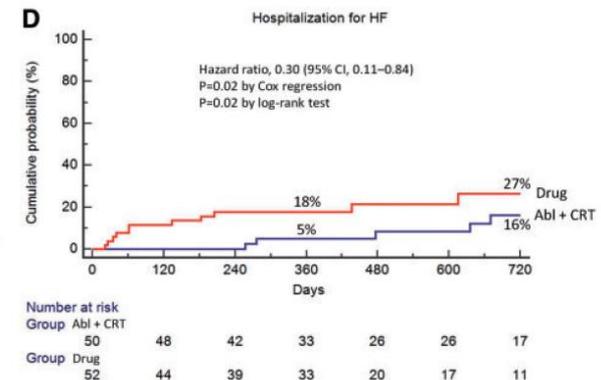
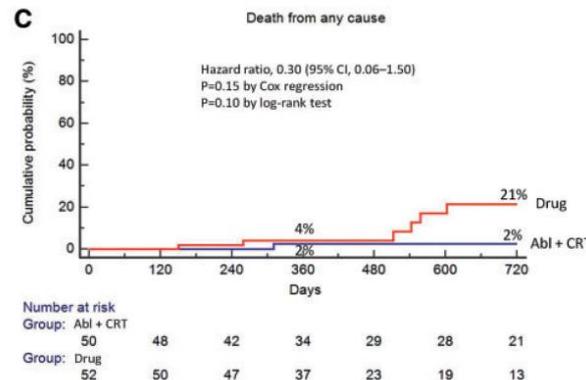
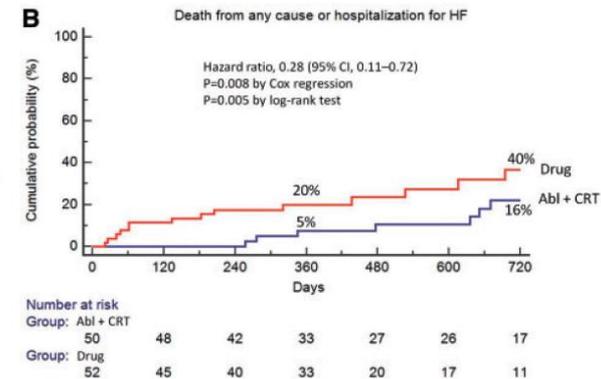
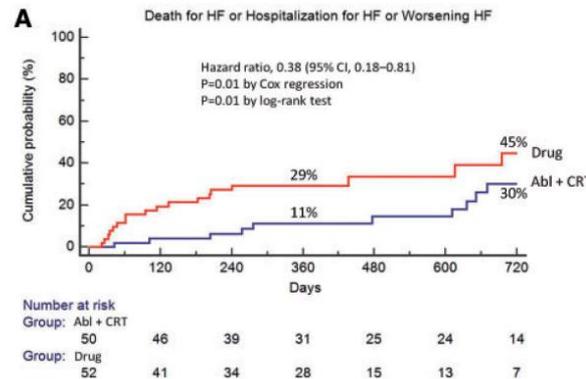
AVNA + CRT = superior to medical therapy

Absolute risk reduction of 18%

NNT= 5.5

## A randomized controlled trial of atrioventricular junction ablation and cardiac resynchronization therapy in patients with permanent atrial fibrillation and narrow QRS

Michele Brignole<sup>1\*</sup>, Evgeny Pokushalov<sup>2</sup>, Francesco Pentimalli<sup>3</sup>, Pietro Palmisano<sup>4</sup>, Enrico Chieffo<sup>5</sup>, Eraldo Occhetta<sup>6</sup>, Fabio Quartieri<sup>7</sup>, Leonardo Calò<sup>8</sup>, Andrea Ungar<sup>9</sup>, and Lluis Mont<sup>10</sup>; for the APAF-CRT Investigators<sup>1</sup>



# Pace and ablate

## APAF-CRT

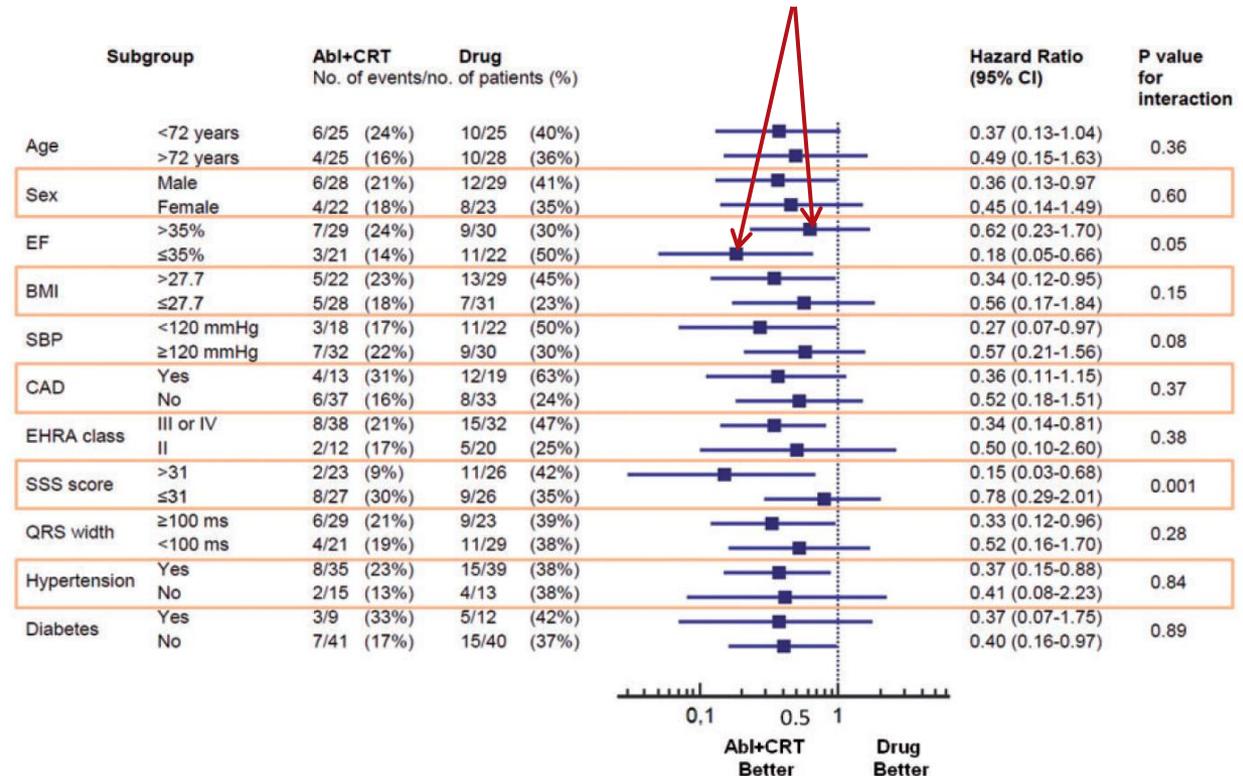
Optimal medical therapy vs. AVN ablation in CRT/permanent AF  
*narrow QRS complex*

hospitalized for HF in last 12 months

Reduction in *harder endpoints* is expected to be more marked in those with *reduced EF*

A randomized controlled trial of  
 atrioventricular junction ablation and cardiac  
 resynchronization therapy in patients with  
 permanent atrial fibrillation and narrow QRS

Michele Brignole<sup>1\*</sup>, Evgeny Pokushalov<sup>2</sup>, Francesco Pentimalli<sup>3</sup>, Pietro Palmisano<sup>4</sup>,  
 Enrico Chieffo<sup>5</sup>, Eraldo Occhetta<sup>6</sup>, Fabio Quartieri<sup>7</sup>, Leonardo Calò<sup>8</sup>,  
 Andrea Ungar<sup>9</sup>, and Lluís Mont<sup>10</sup>; for the APAF-CRT Investigators<sup>1</sup>



# AF catheter ablation OR CRT + AV node ablation?

## PABA-CHF

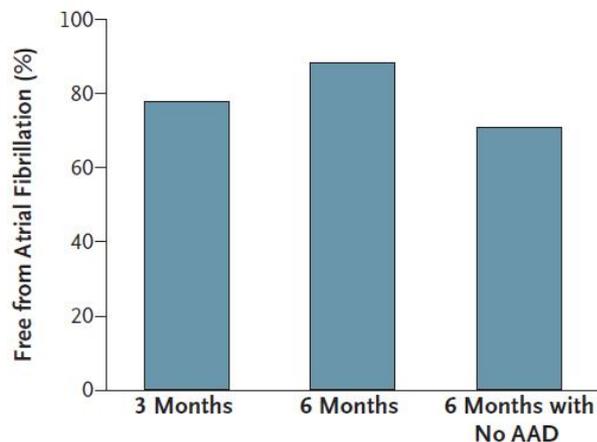
### AF ablation (PVI) vs. CRT+AVN ablation

AF, EF<40%, NYHA II-III

FU 6 months, SR:

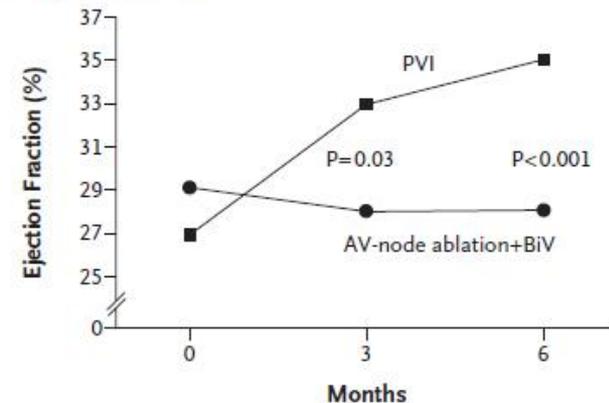
88% with AA

71% without AA

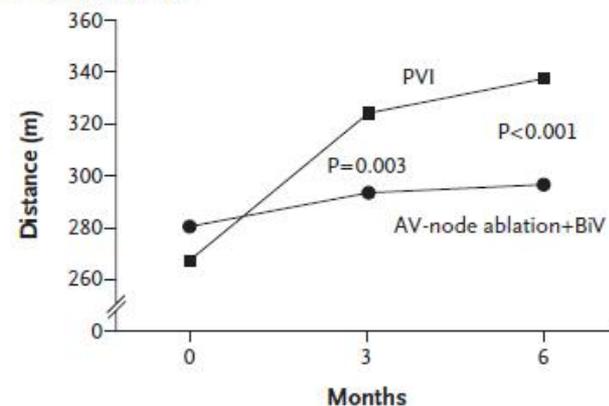


In a direct comparison, AF ablation is better than CRT+AVN ablation

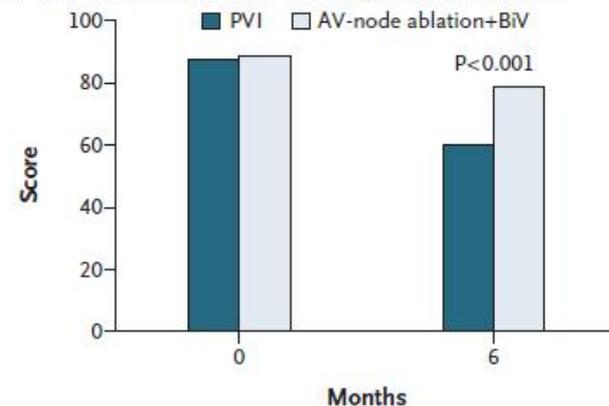
### A Ejection Fraction



### B 6-Minute Walk



### C Minnesota Living with Heart Failure Questionnaire



# Clinical guidance to the choice of treatment in patients with AF and HFrEF

## Factors favouring AF ablation

---

Recent onset HF  
Recent onset AF with fast ventricular rates  
Idiopathic CMP  
Ventricular LGE-MRI negative  
LVEF  $\geq 25\%$   
LA diameter  $< 55$  mm  
LA fibrosis (LGE-MRI)  $\leq 10\%$   
Young patients ( $< 65$  years)  
No/few comorbidities  
Experienced high-volume centre

*Low peri-procedural risk/high benefit*

## Factors favouring medical therapy or pace-and-ablate strategy

---

History of HF  $\gg$  AF  
Long-standing persistent AF with controlled ventricular rates  
Ischaemic or valvular CMP  
Ventricular LGE-MRI positive  
LVEF  $< 25\%$   
LA diameter  $\geq 55$  mm  
LA fibrosis (LGE-MRI)  $> 10\%$   
Elderly patients ( $\geq 80$  years)  
Major comorbidities  
Less experienced low-volume centre  
Failed repeat ablation of persistent AF

*High peri-procedural risk/low benefit*

## Tachycardia-induced CMP?

- Should always be considered in patients with **new-onset or worsening HF** in the setting of AF with **rapid ventricular response**, particularly in those without prior history of ischemic or structural heart disease
- Not only rapid but also normal irregular ventricular responses can lead to TCM (alike VPBs), *pharmacological rate control alone may not be sufficient*

## Cardioversion....6-8 weeks (SR)...reevaluate TTE

- The **greatest clinical benefit from restored sinus rhythm**
- We can avoid unnecessary long-term medical or device-based treatment for HF, improve prognosis

# Ventricular premature beats ablation

RFA of PVCs ↑ LVEF in patients with LV systolic dysfunction

*Takemoto M. J Am Coll Cardiol 2005*

Benefit of PVC suppression originally described in suspected PVC-induced CMP  
(elimination of the primary cause)

*Chugh SS, J Cardiovasc Electrophysiol 2000*

Recent studies - PVC ablation ↑ LV systolic function in other clinical scenarios  
(post-MI, CRT-non-responders, non-ischemic CMP)

*Sarrazin JF. Heart Rhythm 2009*

*Lakkireddy D, J Am Coll Cardiol 2012*

Lowest PVC burden associated with LV dysfunction = 4%

*Shanmugam N, Eur J Heart Fail 2006*

# Ventricular premature beats ablation

Mean improvement of 12% in LVEF after PVC ablation in patients with frequent PVC and LV dysfunction

*Mountantonakis. Heart Rhythm 2011*

...superior to that achieved by other heart failure treatments, as for example ACEi or CRT

*Solomon SD, Circulation 2005*

*St John Sutton MG, Circulation 2003*

... comparable to that obtained with beta-blocker therapy

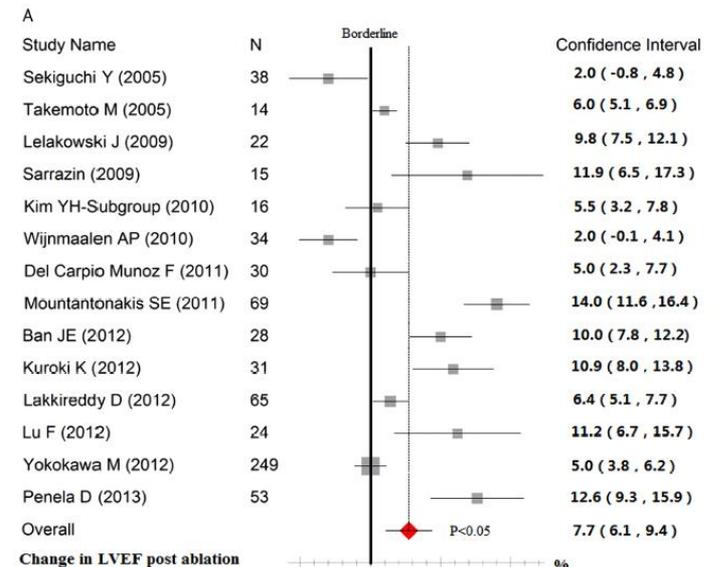
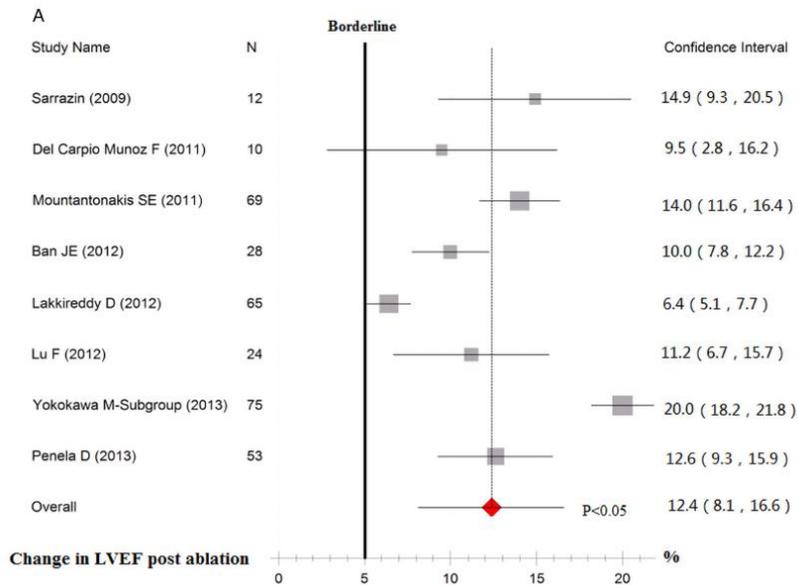
*De Groote P, Am Heart J 2007*

increases the efficacy of CRT

*Lakkireddy D, J Am Coll Cardiol 2012*

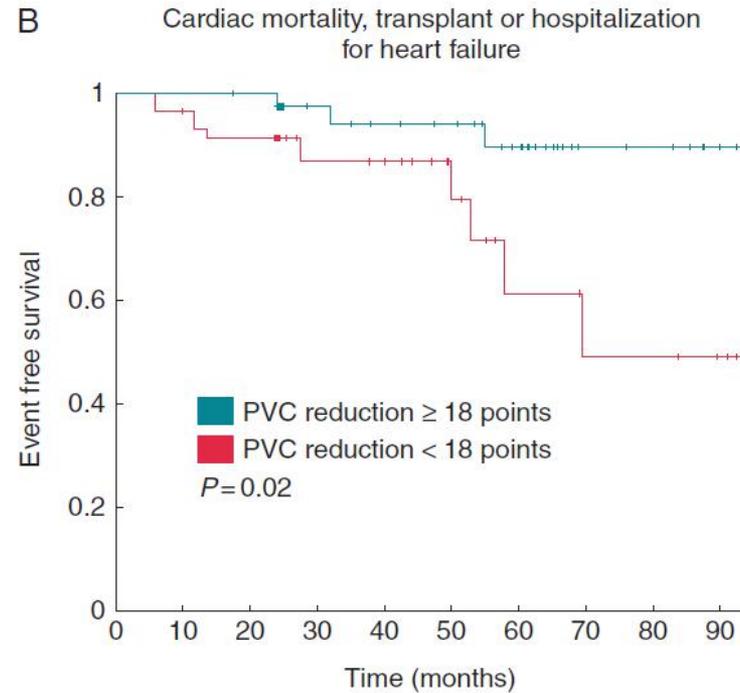
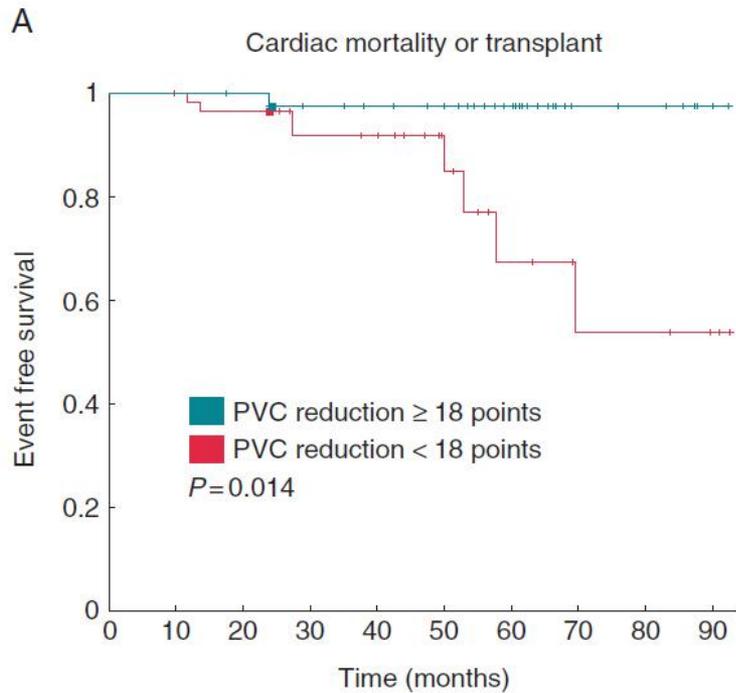
allows for withdrawal of the indication for primary prevention ICD

*Penela D, Heart Rhythm 2015*



# Ventricular premature beats ablation

**Good outcome after PVC ablation** not only in tachycardia-induced CMP  
but also in an unselected population of patients with LV systolic dysfunction



# Conclusion

- Catheter ablation can safely be performed with acceptable complication rates in patients with HFrEF
- Compared with standard drug therapy, catheter ablation of AF in patients with HFrEF reduces all-cause mortality and HF hospitalization and improves LVEF, functional capacity, and quality of life
- Little evidence is available to support that CRT is effective in patients with permanent AF without AVN ablation – maximize CRT! – not suitable for complex ablation? – AVN ablation
- PVC ablation indication should be done rather according to PVC burden and not the supposed etiology

Thank you  
for your attention

