Advances in Cardiac Arrhhythmias and Great Innovations in Cardiology
Torino, 13/15 Ottobre 2016

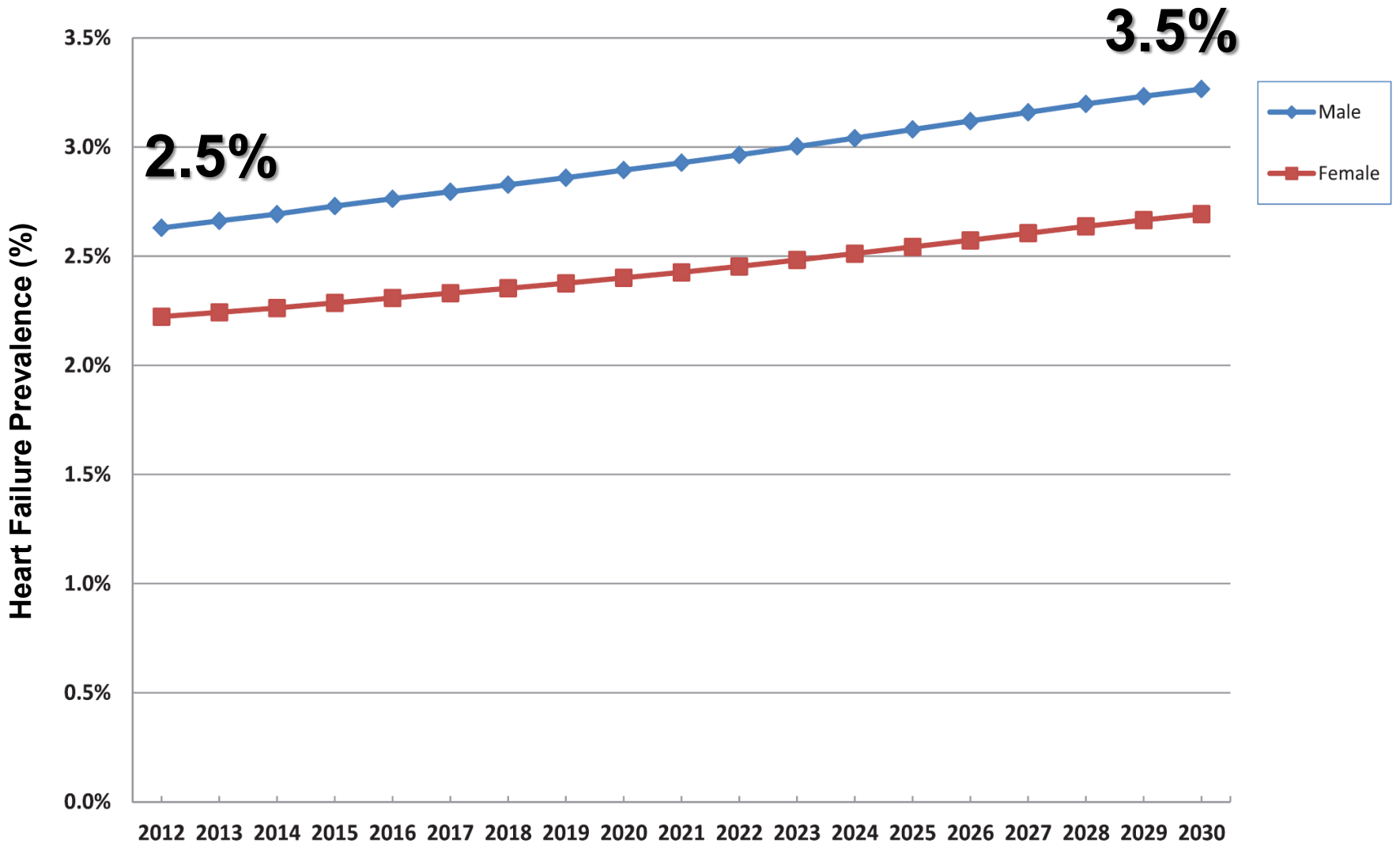
# How atrial fibrillation should be treated in the heart failure patient?


**Matteo Anselmino**
Dipartimento Scienze Mediche
"Città della Salute e della Scienza" Hospital
University of Turin, Italy

**Disclosure:**

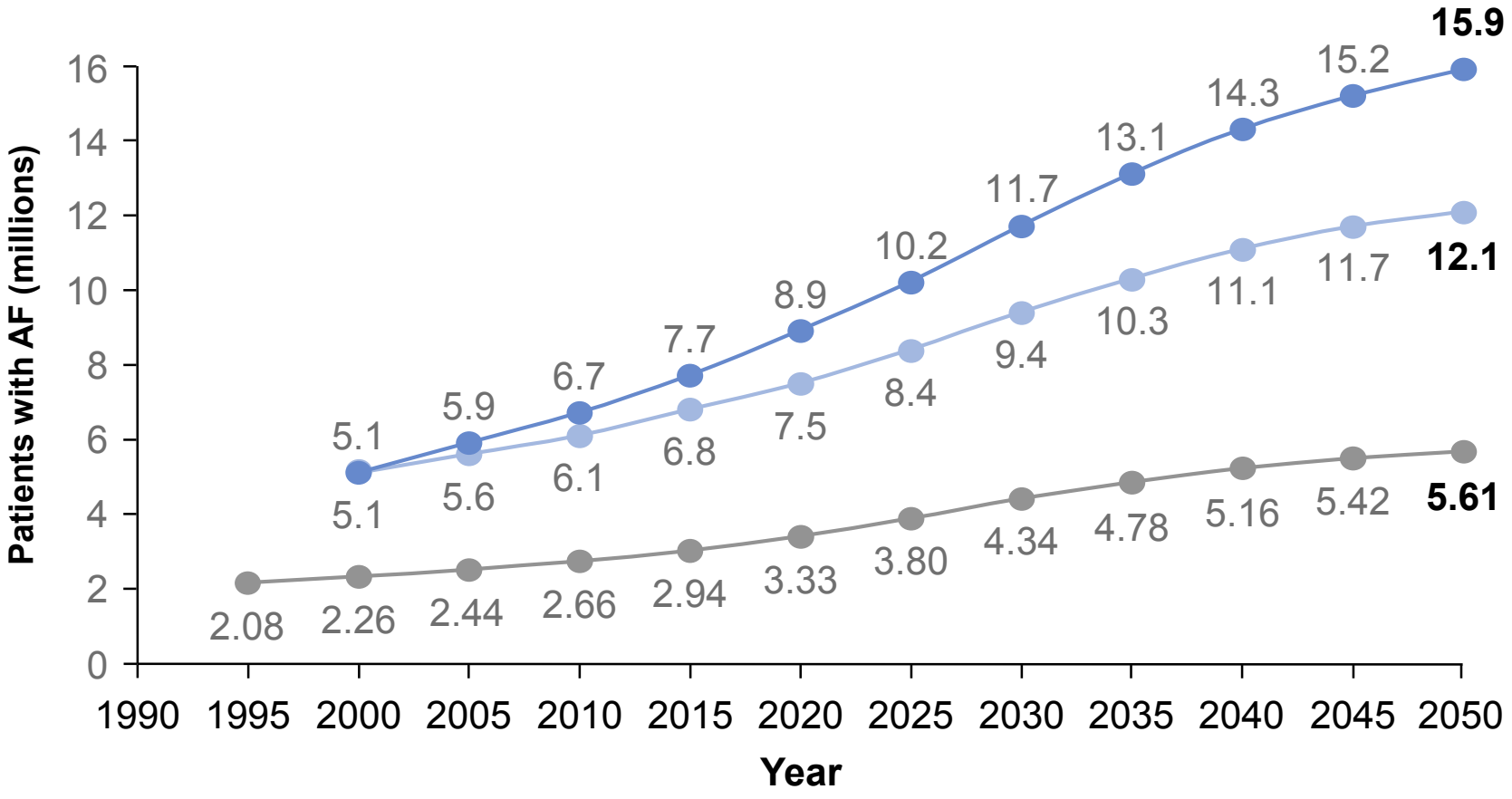
Honoraria (**lecture fees**) from St. Jude Medical and Biosense Webster

# HF Epidemiology - Prevalence




Heidenreich PA et al. *Circ Heart Fail* 2013; 6:606-19

# AF Epidemiology - Prevalence




Olmsted County data, 2006[1] (assuming a continued increase in AF incidence)

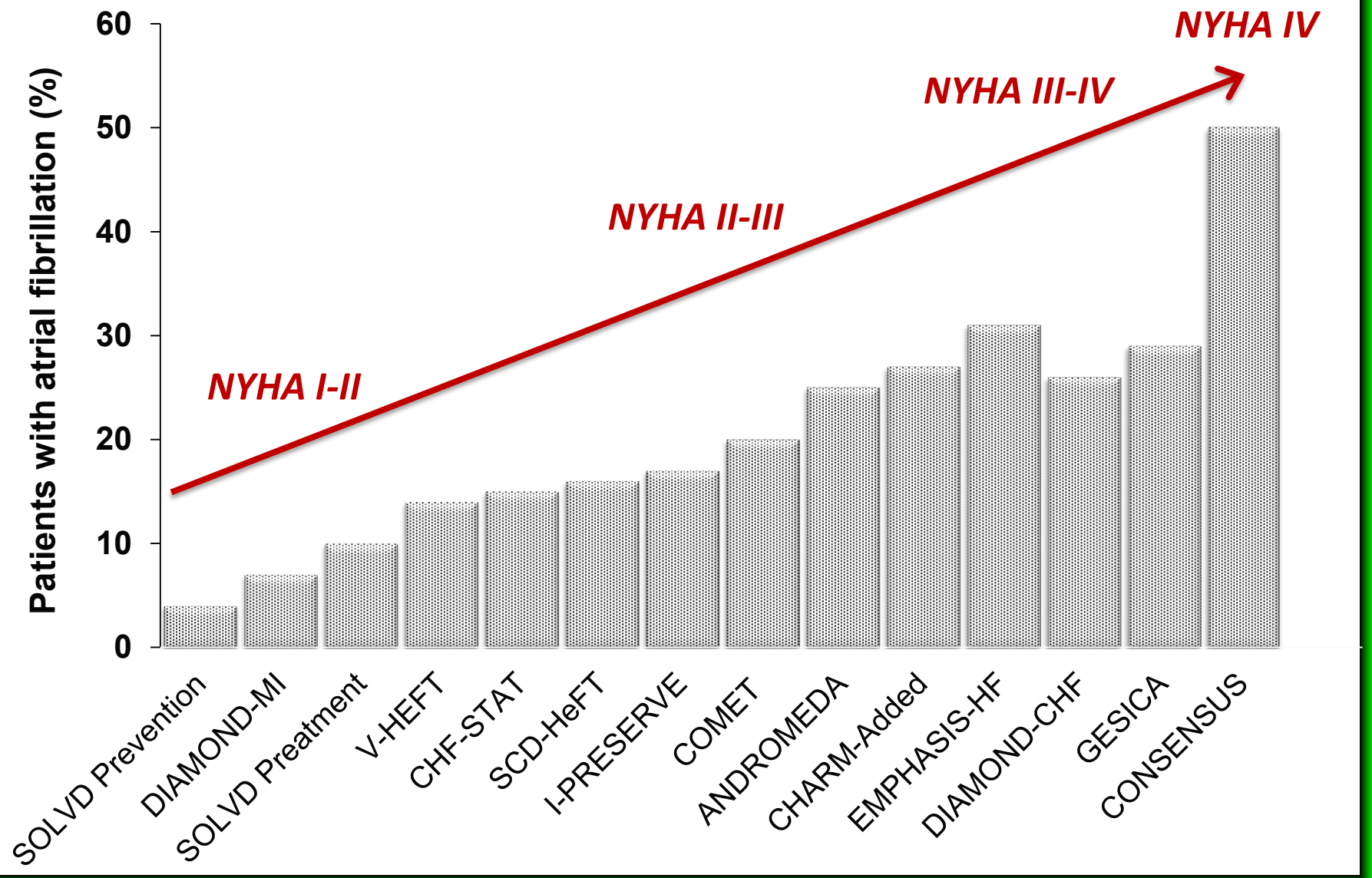
Olmsted County data, 2006[1] (assuming no further increase in AF incidence)

ATRIA study data, 2000[2]

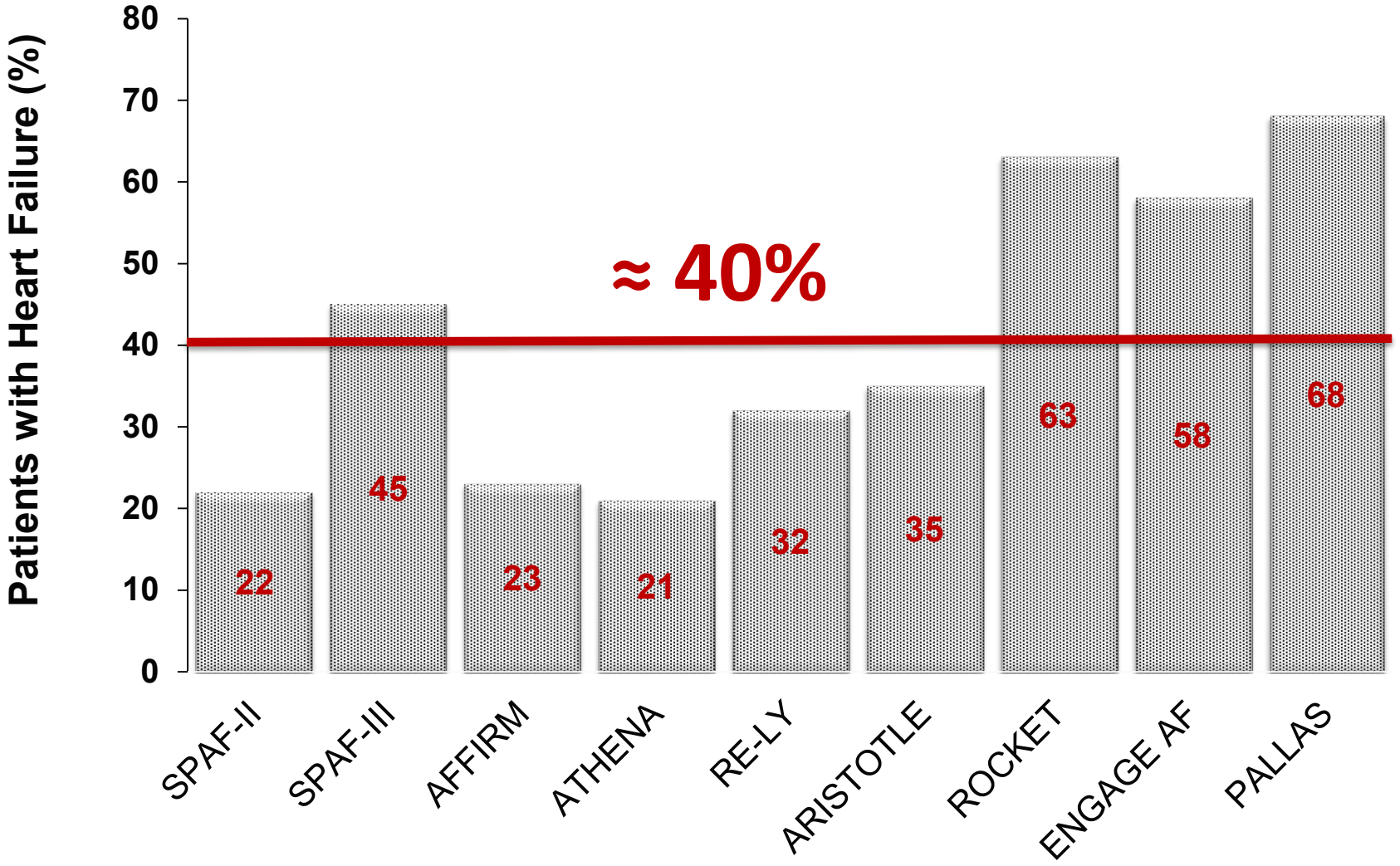

Miyasaka Y et al. Circulation. 2006;114(2):119–125

Go AS et al. JAMA. 2001;285(18):2370–2375

# Prevalence of AF in HF Trials



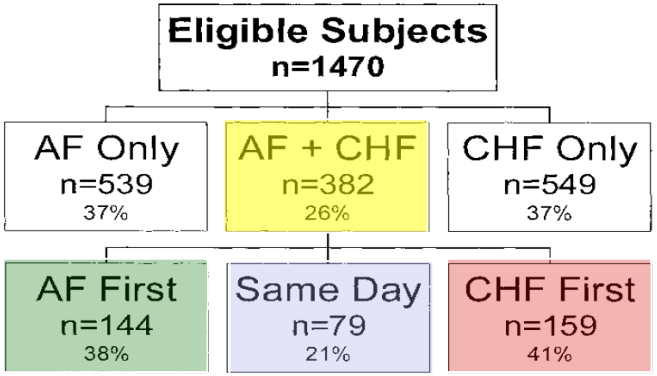
# Prevalence of HF in Selected AF Trials



# Prognostic Impact of AF and HF

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

### The Framingham Heart Study




**Pts with AF or HF who develop the other condition have poor prognosis**

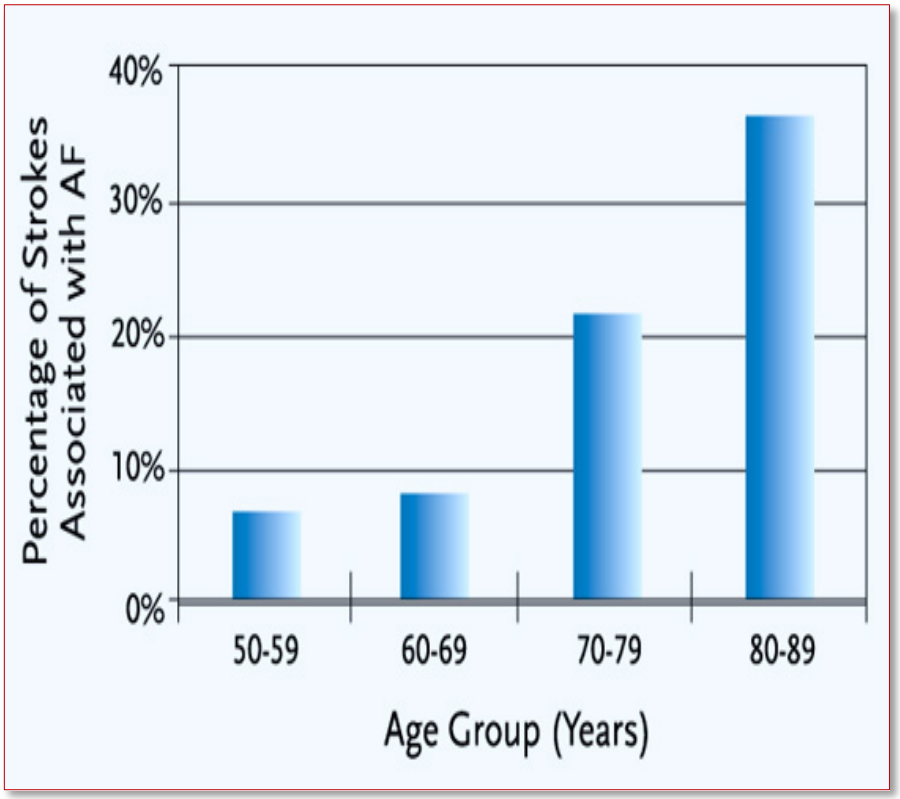
Comorbid condition as a time-dependent variable

| | | |
|---|---|---|
| (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

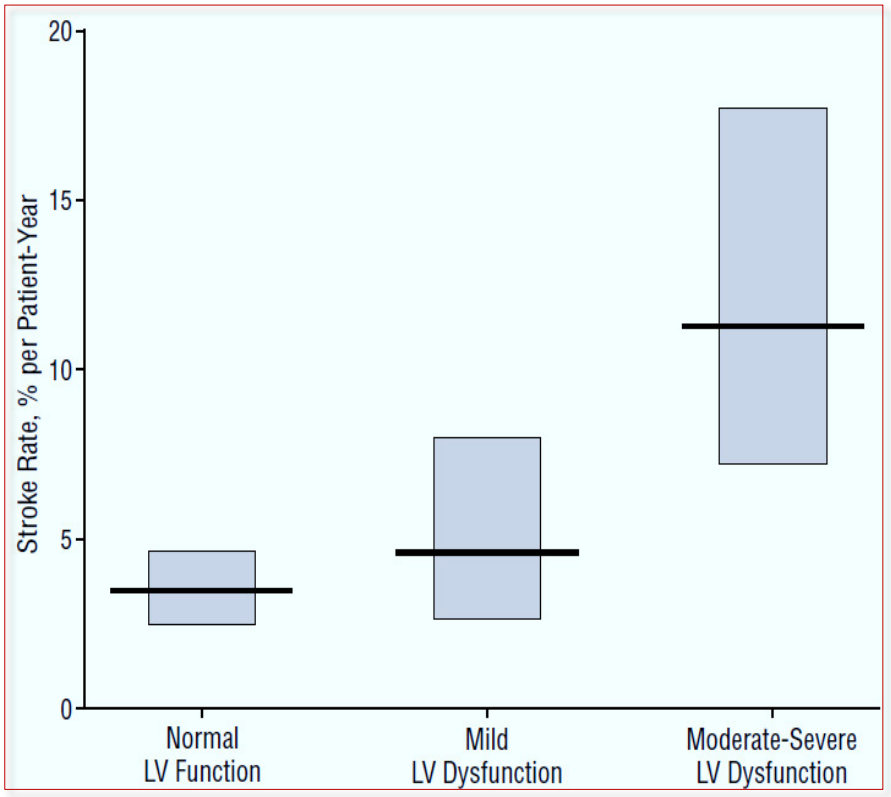
# Thromboembolic Risk in AF and HF

**Atrial fibrillation**
**↑ 5-fold the risk of stroke**




Wolf PA et al, *Arch Intern Med.* 1987; 147: 1561-1564

**Moderate-to-severe LVSD**
**↑ 2.5-fold the risk of stroke**




AF Investigators. *Arch Intern Med.* 1988; 158: 1316-1320

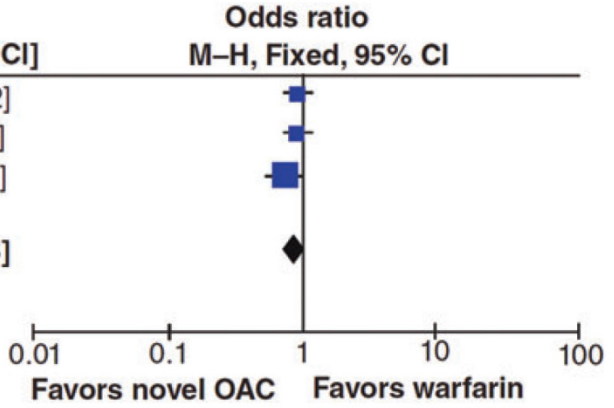
# Novel Oral Anticoagulants (NOACs) in HF

## Patients with Heart Failure

A

| Study or subgroup | Novel OAC Events | Total | Warfarin Events | Total | Weight% | Odds ratio M–H, [Fixed, 95% CI] |
|---|---|---|---|---|---|---|
| ARISTOTLE (2011) | 70 | 3235 | 79 | 3216 | 23.1 | 0.88 [0.63, 1.22] |
| RE-LY (2009) | 130 | 3871 | 71 | 1922 | 27.3 | 0.91 [0.67, 1.22] |
| ROCKET-AF (2011) | 160 | 4438 | 172 | 4413 | 49.6 | 0.92 [0.74, 1.15] |
| **Total (95% CI)** | | **11544** | | **9551** | **100.0** | **0.91 [0.78, 1.06]** |
| Total events | 360 | | 322 | | | |

Heterogeneity: Chi² = 0.06, df = 2 (p = 0.97); I² = 0%
Test for overall effect: Z = 1.23 (p = 0.22)

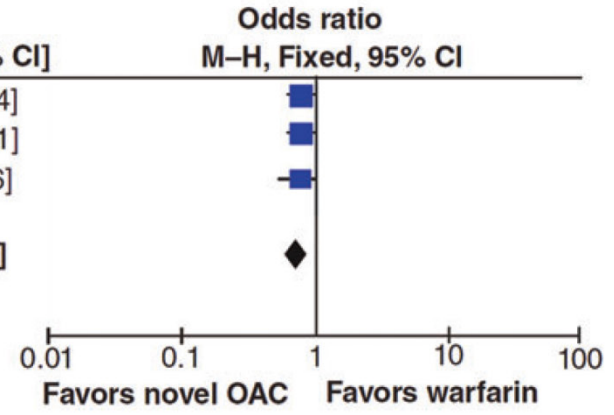



## In patients with HF → NOACS non-inferior to Warfarin

B

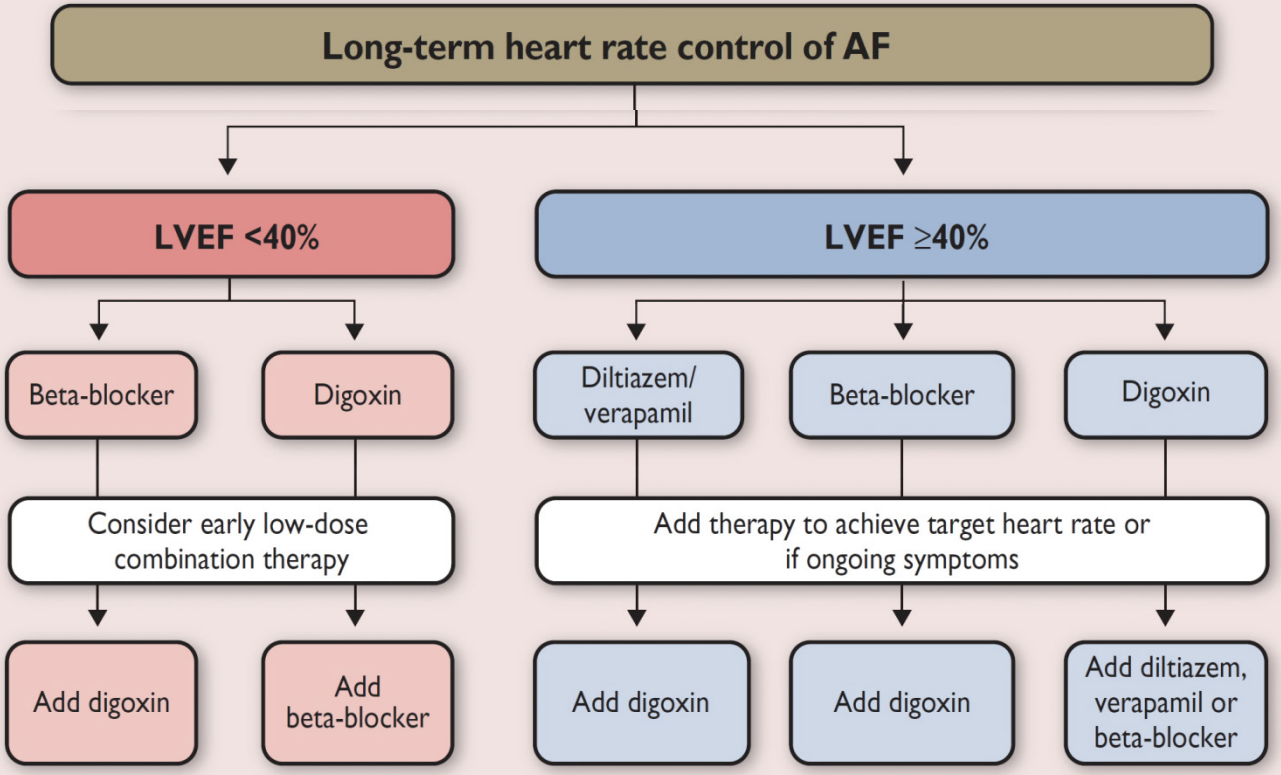
| Study or subgroup | Novel OAC Events | Total | Warfarin Events | Total | Weight% | Odds ratio M–H, [Fixed, 95% CI] |
|---|---|---|---|---|---|---|
| ARISTOTLE (2011) | 142 | 5885 | 186 | 5865 | 37.6 | 0.75 [0.30, 0,94] |
| RE-LY (2009) | 197 | 8220 | 134 | 4100 | 36.1 | 0.73 [0.58, 0,91] |
| ROCKET-AF (2011) | 109 | 2642 | 134 | 2676 | 26.4 | 0.82 [0.63, 1.06] |
| **Total (95% CI)** | | **16747** | | **12641** | **100.0** | **0.76 [0.67, 0.87]** |
| Total events | 448 | | 454 | | | |

Heterogeneity: Chi² = 0.45, df = 2 (p = 0.80); I² = 0%
Test for overall effect: Z = 3.98 (p = 0.0001)




Ahmad et al. *Expert Rev Cardiovasc Ther* 2012; 10:1471-1480

# Pharmacological rate control in patients with HF and concomitant AF



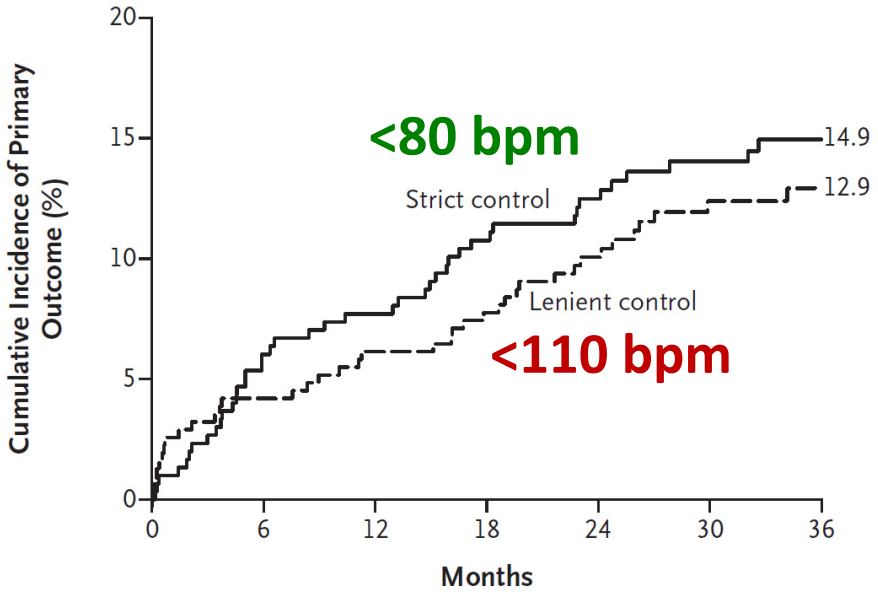

2016 ESC Guidelines for the management of AF. Eur Heart J 2016; Aug 27

# Rate control – Heart Rate Target

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 15, 2010 VOL. 362 NO. 15

## Lenient versus Strict Rate Control in Patients with Atrial Fibrillation



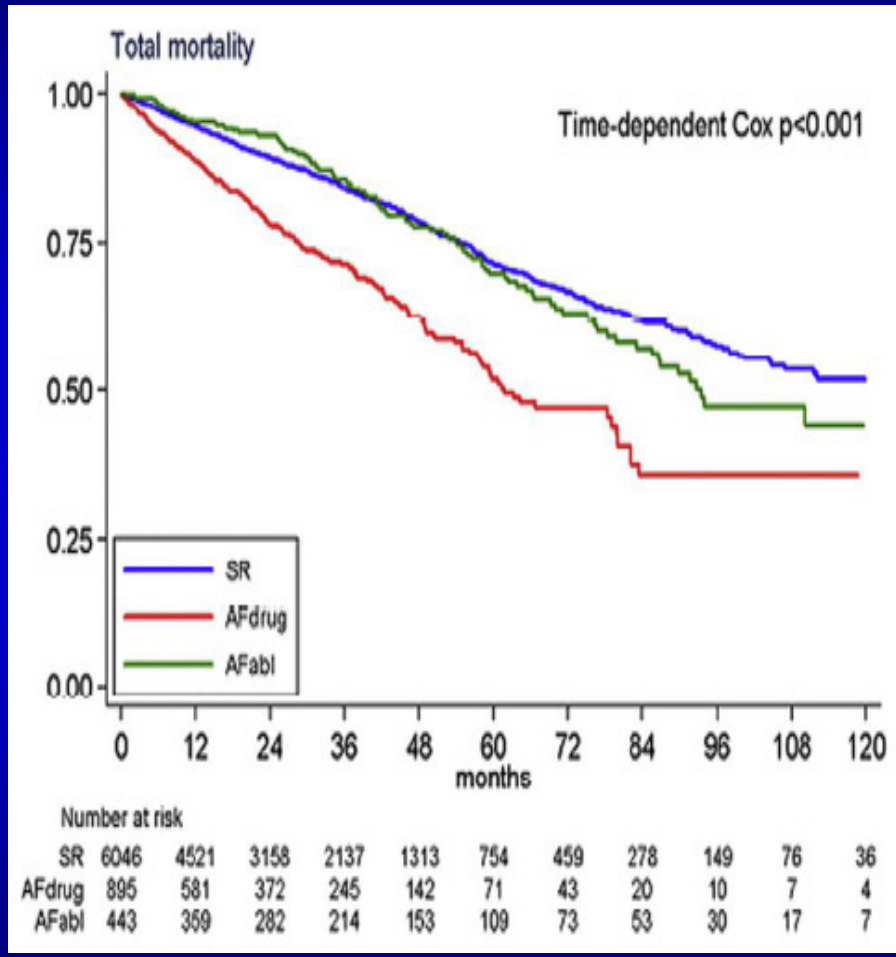

HR 0.84 (0.58-1.21)

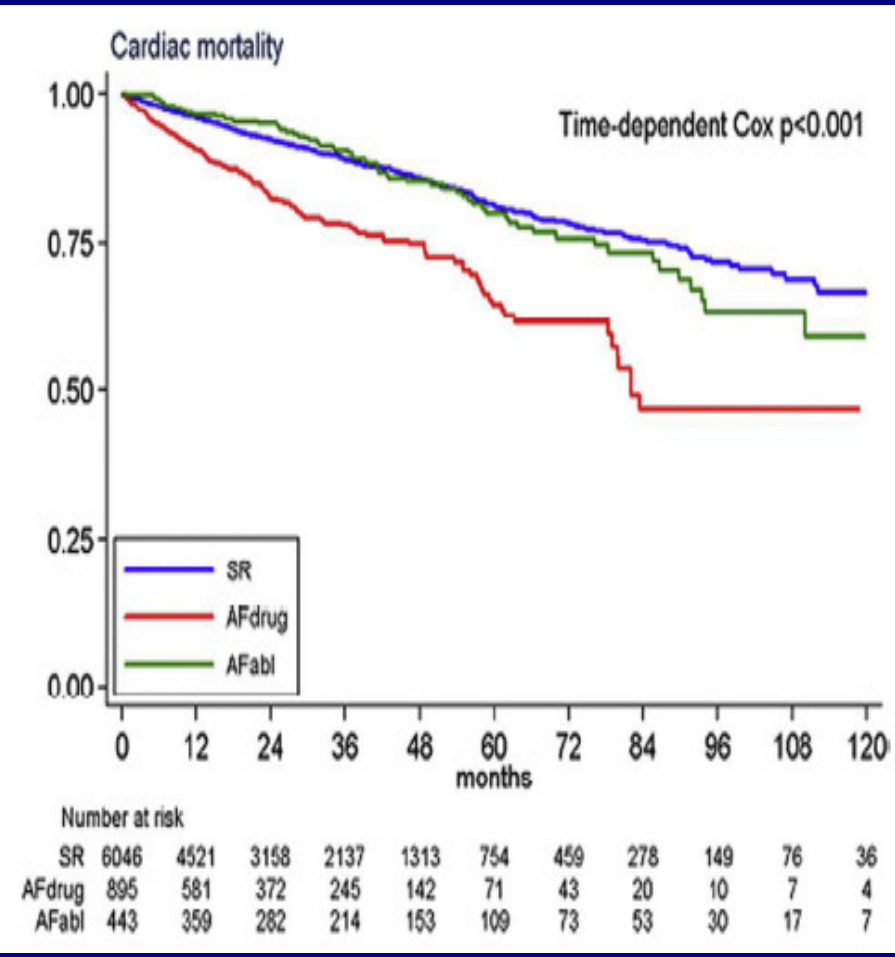
| No. at Risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| Strict control | 303 | 282 | 273 | 262 | 246 | 212 | 131 |
| Lenient control | 311 | 298 | 290 | 285 | 255 | 218 | 138 |

# Interventional approaches to obtain rate control in AF patients with heart failure

- AV node ablation + RV pacing (1990)
- AV node ablation + CRT (2000)

# CRT + AV ablation vs Drugs CERTIFY study




Gasparini JACC Heart Fail 2013

# Atrial fibrillation and heart failure

Triggered activity

Heterogeneous conduction

Atrial fibrosis

Atrial stretch

Pressure and volume overload

~~Atrial fibrillation~~

Heart failure

Fast ventricular rate

Irregular cycles

Loss of atrial contraction

Mitral and tricuspid regurgitation

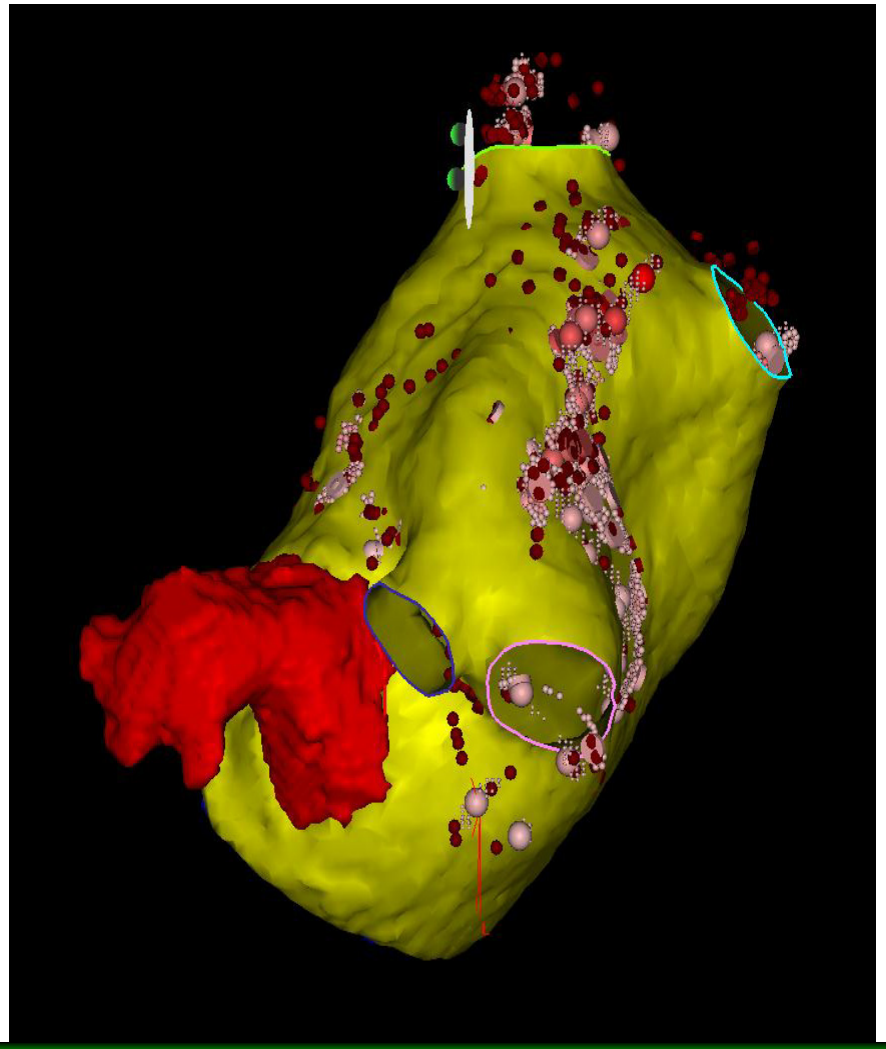
# Options for Pharmacological Rhythm Control in Patients with AF and HF

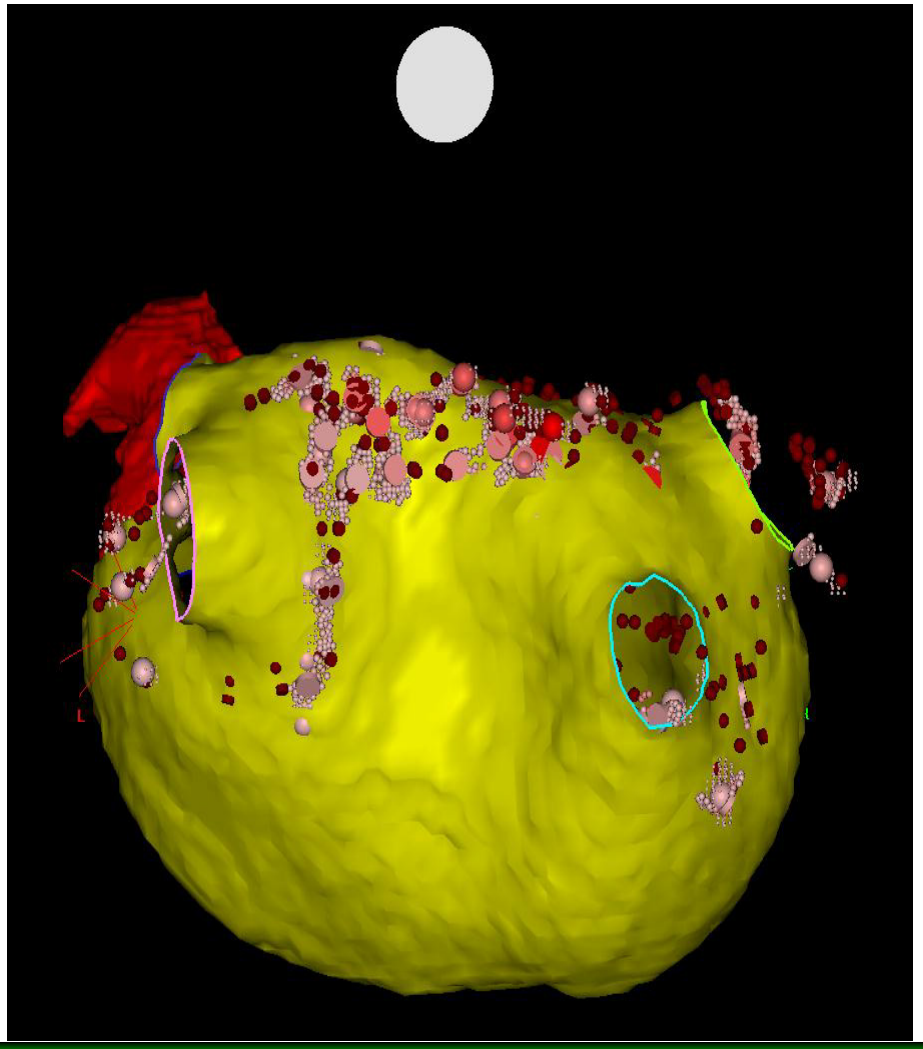
- **Amiodarone**
- **Dofetilide** (not approved in EU, risk of TdP)
- **Dronedarone** (restricted use after ANDROMEDA)

| | | |
|---|---|---|
| Dronedarone is not recommended because of an increased risk of hospital admissions for cardiovascular causes and an increased risk of premature death in NYHA Class III-IV patients | III | A |

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic HF. Eur Heart J 2016; Aug 27

# Transcatheter Atrial Fibrillation Ablation in patients with Heart Failure



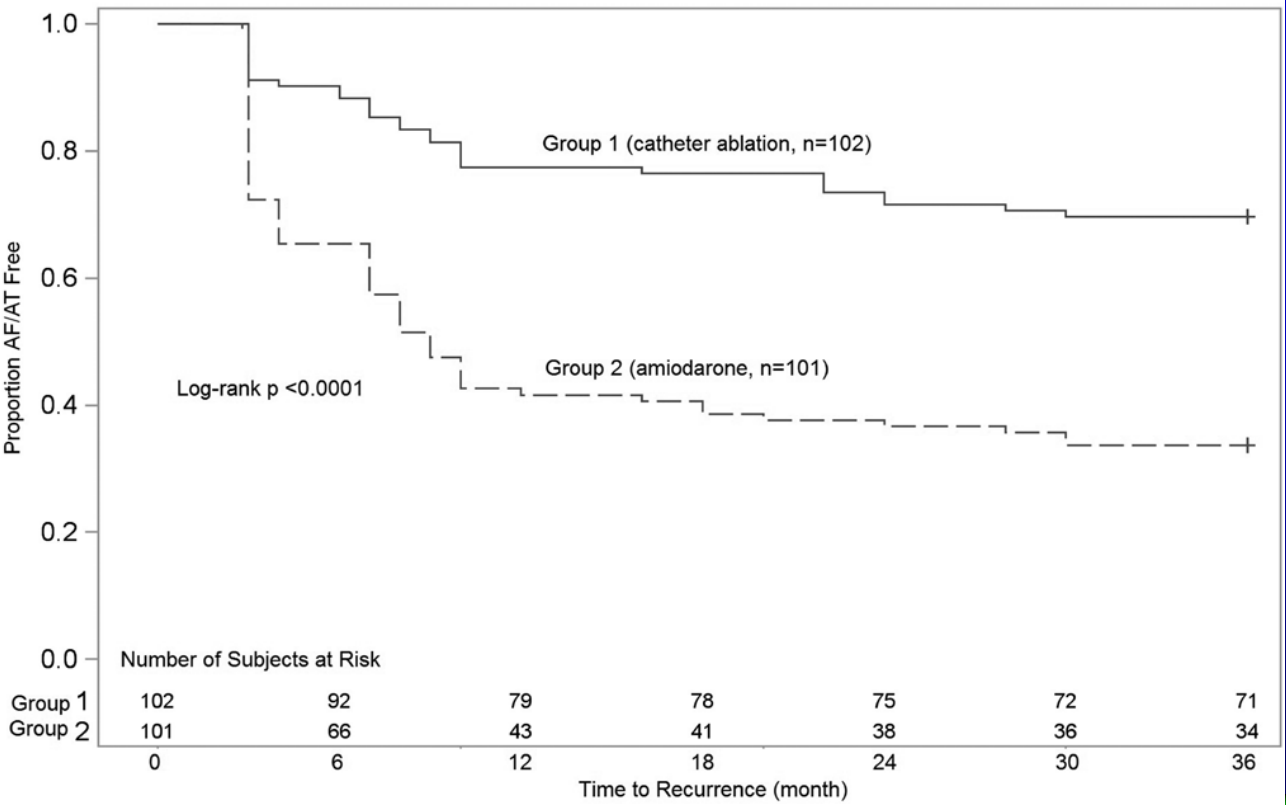


# Ablation Versus Amiodarone for Treatment of Persistent Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted Device

## Results From the AATAC Multicenter Randomized Trial

Luigi Di Biase, MD, PhD; Prasant Mohanty, MBBS, MPH; Sanghamitra Mohanty, MD; Pasquale Santangeli, MD; Chintan Trivedi, MD, MPH; Dhanunjaya Lakkireddy, MD; Madhu Reddy, MD; Pierre Jais, MD; Sakis Themistoclakis, MD; Antonio Dello Russo, MD; Michela Casella, MD; Gemma Pelargonio, MD; Maria Lucia Narducci, MD; Robert Schweikert, MD; Petr Neuzil, MD; Javier Sanchez, MD; Rodney Horton, MD; Salwa Beheiry, RN; Richard Hongo, MD; Steven Hao, MD; Antonio Rossillo, MD; Giovanni Forleo, MD; Claudio Tondo, MD; J. David Burkhardt, MD; Michel Haissaguerre, MD; Andrea Natale, MD

Circulation. 2016 Apr 26;133(17)



# PABA-CHF Randomized Trial

Symptomatic AF, HF NYHA II/III, LVEF≤40%, On BB/ACE (spironolactone) for NYHA III

81 Underwent randomization

| Pulmonary vein isolation (41 pts) | |
|---|---|
| Paroxysmal AF | **49%** |
| Persistent / LSP AF | **51%** |
| AF Duration (yr) | **4.0 ± 2.4** |
| LVEF (%) | **27 ± 8** |

| AV node ablation + biventricular pacing (40 pts) | |
|---|---|
| Paroxysmal AF | 54% |
| Persistent / LSP AF | 46% |
| AF Duration (yr) | 3.9 ± 2.8 |
| LVEF (%) | 29 ± 7 |

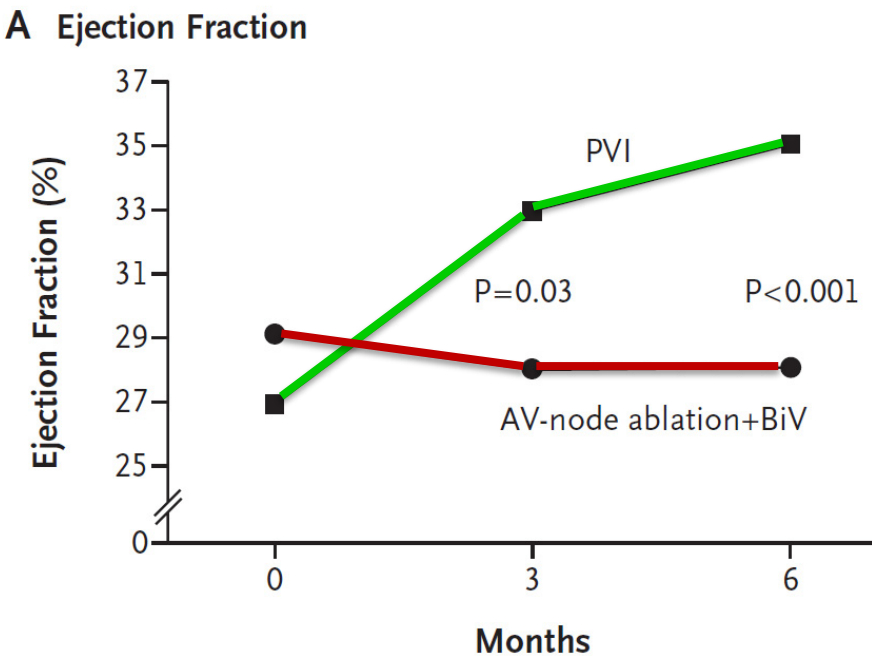
Primary composite end point of **EF**, **distance on 6-min walk test** and **MLWHF score**

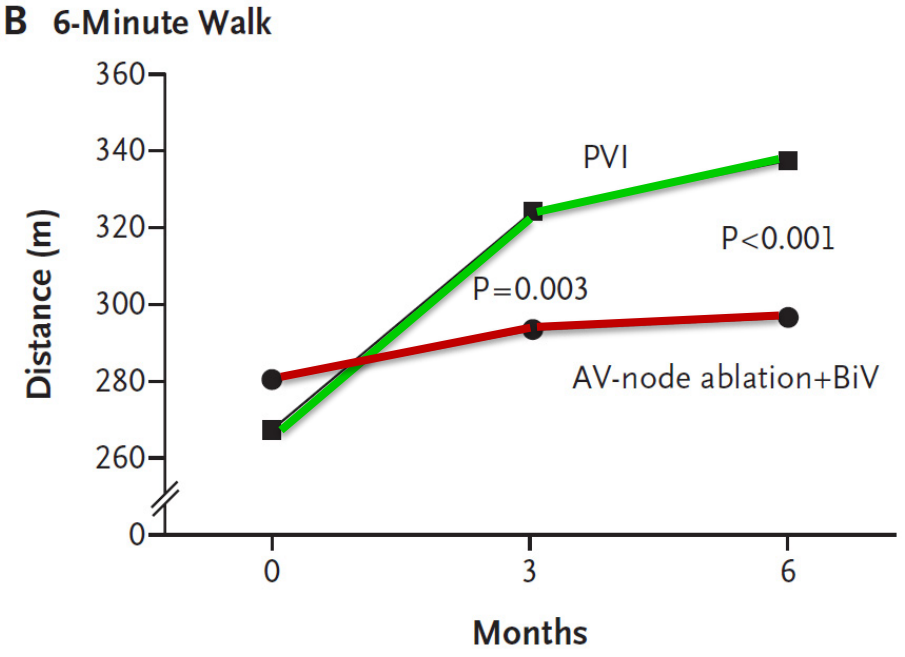
Khan et al. *NEJM* 2008;359:1778-85

# PABA-CHF – 6 Months Follow-Up

**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 Patients with Reduced LVEF

| Author, Year (Ref) | N. pts | FU months | Success single (%) | Redo (%) | Success final (%) | LVEF (%) Changes |
|---|---|---|---|---|---|---|
| Chen 2004 | 94 | 14 | 52 | 22 | 73 | 36→41 |
| Hsu 2004 | 58 | 12 | 28 | 50 | 78 | 35→56 |
| Tondo 2006 | 40 | 14 | 55 | 33 | 87 | 33→47 |
| Gentlesk 2007 | 67 | 6 | 55 | 31 | 86 | 42→56 |
| Nademanee 2008 | 129 | 27 | - | 21 | 79 | 30→37 |
| Lutomsky 2008 | 18 | 6 | 50 | - | - | 41→52 |
| De Potter 2010 | 36 | 16 | 50 | 31 | 69 | 41→58 |
| Cha 2011 | 111 | 12 | - | - | 76 | 35→56 |
| Anselmino 2013 | 196 | 46 | 45 | 30 | 62 | 40→50 |
| Calvo 2013 | 36 | 6 | 70 | 31 | 83 | 41→48 |
| Nedios 2014 | 69 | 28 | 40 | 46 | 65 | 33→48 |
| Bunch 2015 | 267 | 60 | 39 | - | - | 27→42 |
| Khan 2008 | 41 | 6 | 71 | 20 | 88 | 27→35 |
| MacDonald 2010 | 22 | 10 | - | 30 | 50 | 36→41 |
| Jones 2013 | 26 | 10 | 69 | 19 | 88 | 21→32 |
| Hunter 2014 | 26 | 6 | 38 | 54 | 81 | 32→40 |

# AF Ablation in Patients with Reduced LVEF

**Multicenter meta-analysis**

- systematic search in PubMed and Cochrane Library
- direct contact whit each center which published long-term data

# Catheter Ablation of Atrial Fibrillation in Patients With Left Ventricular Systolic Dysfunction

## A Systematic Review and Meta-Analysis

## 26 Studies – 1838 Patients

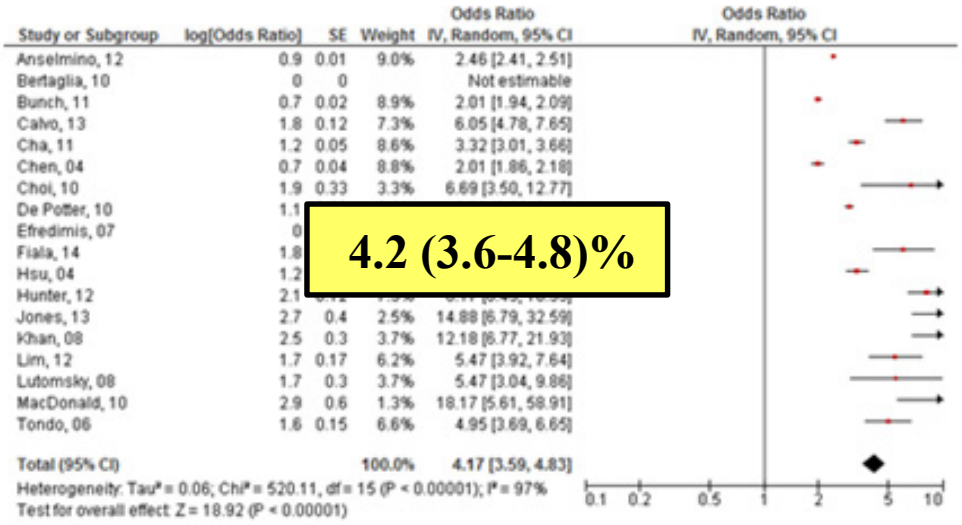
| | *Mean value* | *Lower CI* | *Upper CI* |
|---|---|---|---|
| **Age, years** | **59** | 51 | 61 |
| **Paroxysmal AF, %** | **45** | 41 | 56 |
| **Persistent AF, %** | **50** | 35 | 54 |
| **Long-standing persistent, %** | **5** | 2 | 7 |
| **Time since first AF diagnosis (M)** | **42** | 29 | 46 |
| **Time since first HF diagnosis (M)** | **27** | 20 | 28 |
| **Basal pro-BNP (pg/ml)** | **11,187** | 678 | 11,400 |
| **Cardiomiopathy** | | | |
| **- Ischemic, %** | **41** | 35 | 46 |
| **- Hypertensive, %** | **10** | 5 | 14 |
| **- Valvular heart disease, %** | **10** | 6 | 15 |
| **- Idiopathic, %** | **39** | 35 | 45 |
| **LV ejection fraction, %** | **40** | 35 | 46 |

Anselmino M et al. *Circ Arrhythm Electrophysiol* 2014; 7: 1011-1018

Mean follow-up:

**23 (18-40) months**

A. Procedural complications

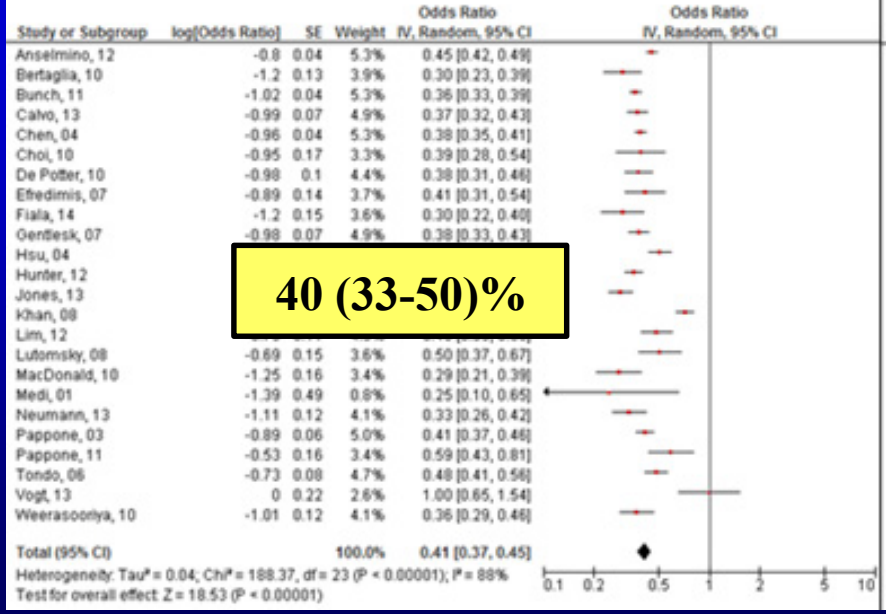



**4.2 (3.6-4.8)%**

Redo procedures:

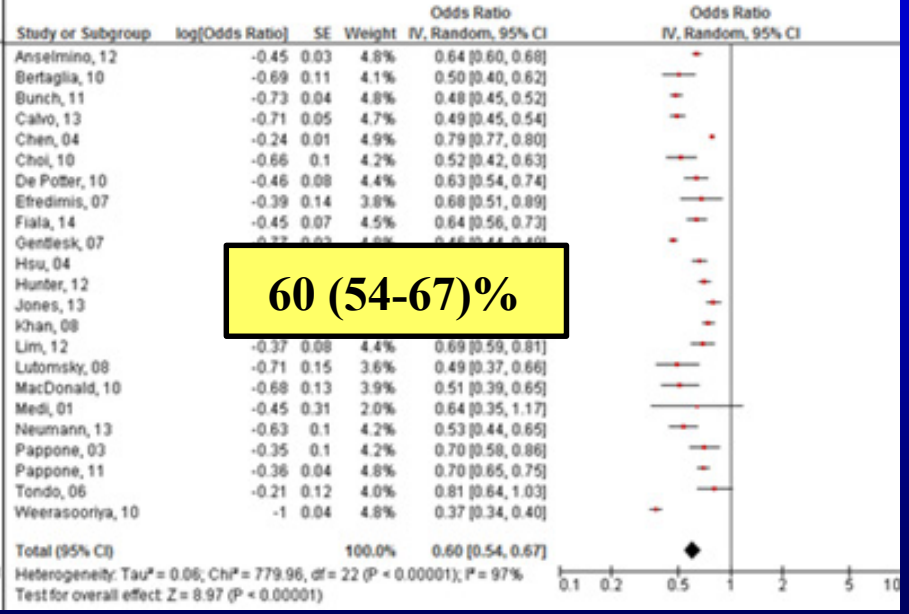
**32 (25-38)%**

B. Catheter ablation efficacy after the first procedure




**40 (33-50)%**

C. Catheter ablation efficacy at the end of follow-up

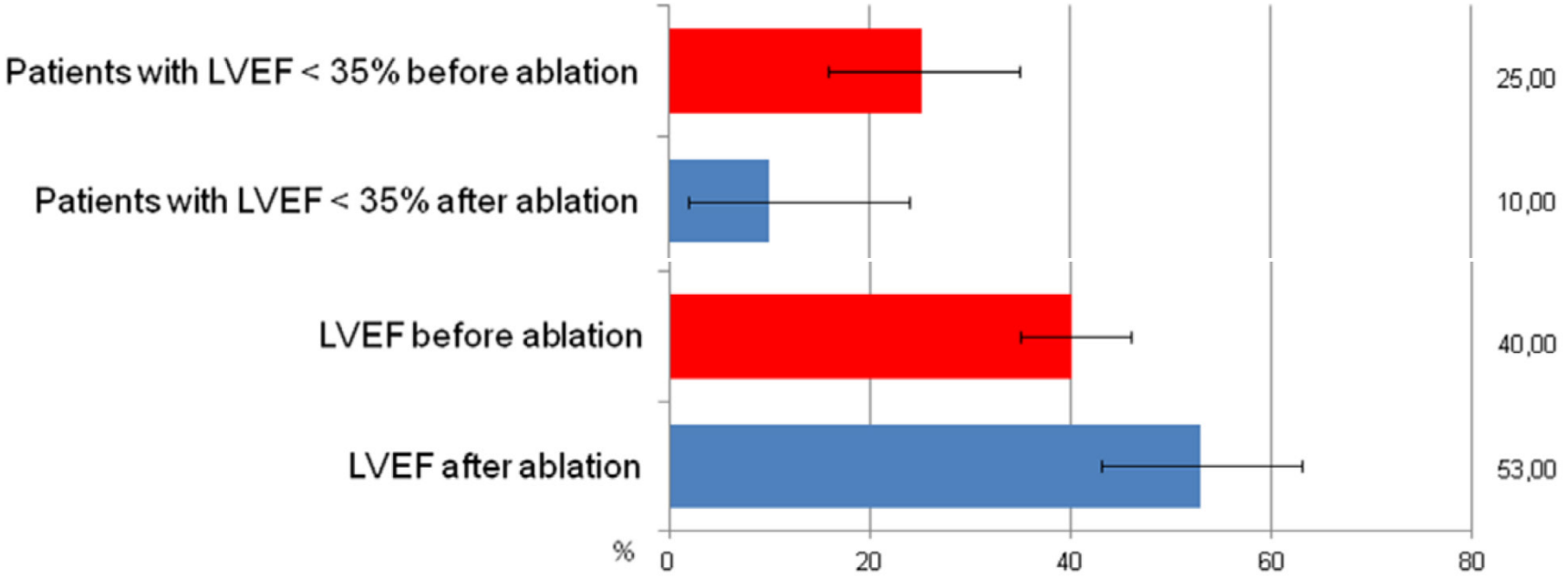



**60 (54-67)%**

# Catheter Ablation of Atrial Fibrillation in Patients With Left Ventricular Systolic Dysfunction

## A Systematic Review and Meta-Analysis

## Impact on Left Ventricular Function



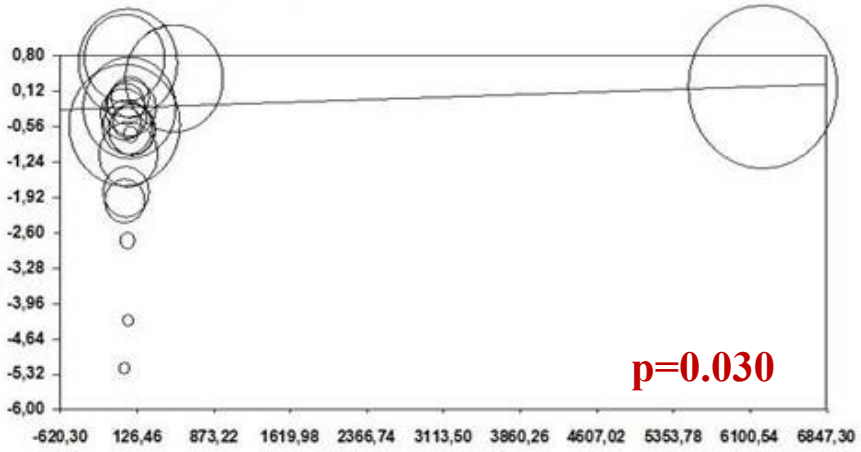

Anselmino M et al. *Circ Arrhythm Electrophysiol* 2014; 7: 1011-1018

# Catheter Ablation of Atrial Fibrillation in Patients With Left Ventricular Systolic Dysfunction

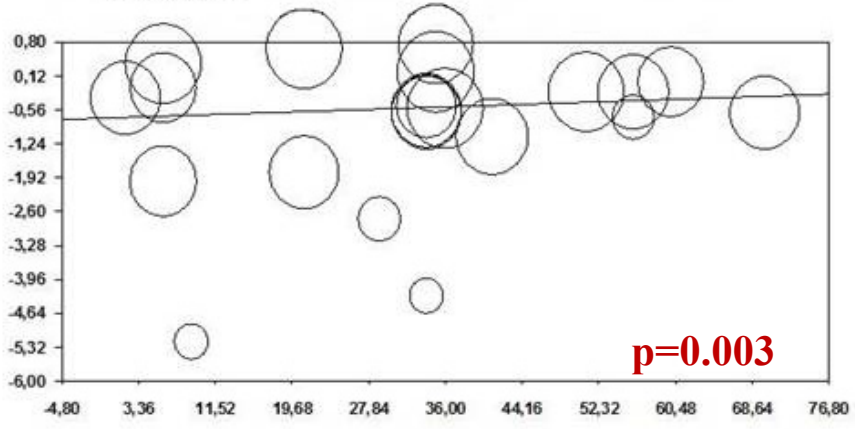
## A Systematic Review and Meta-Analysis

## Predictors of AF Recurrence

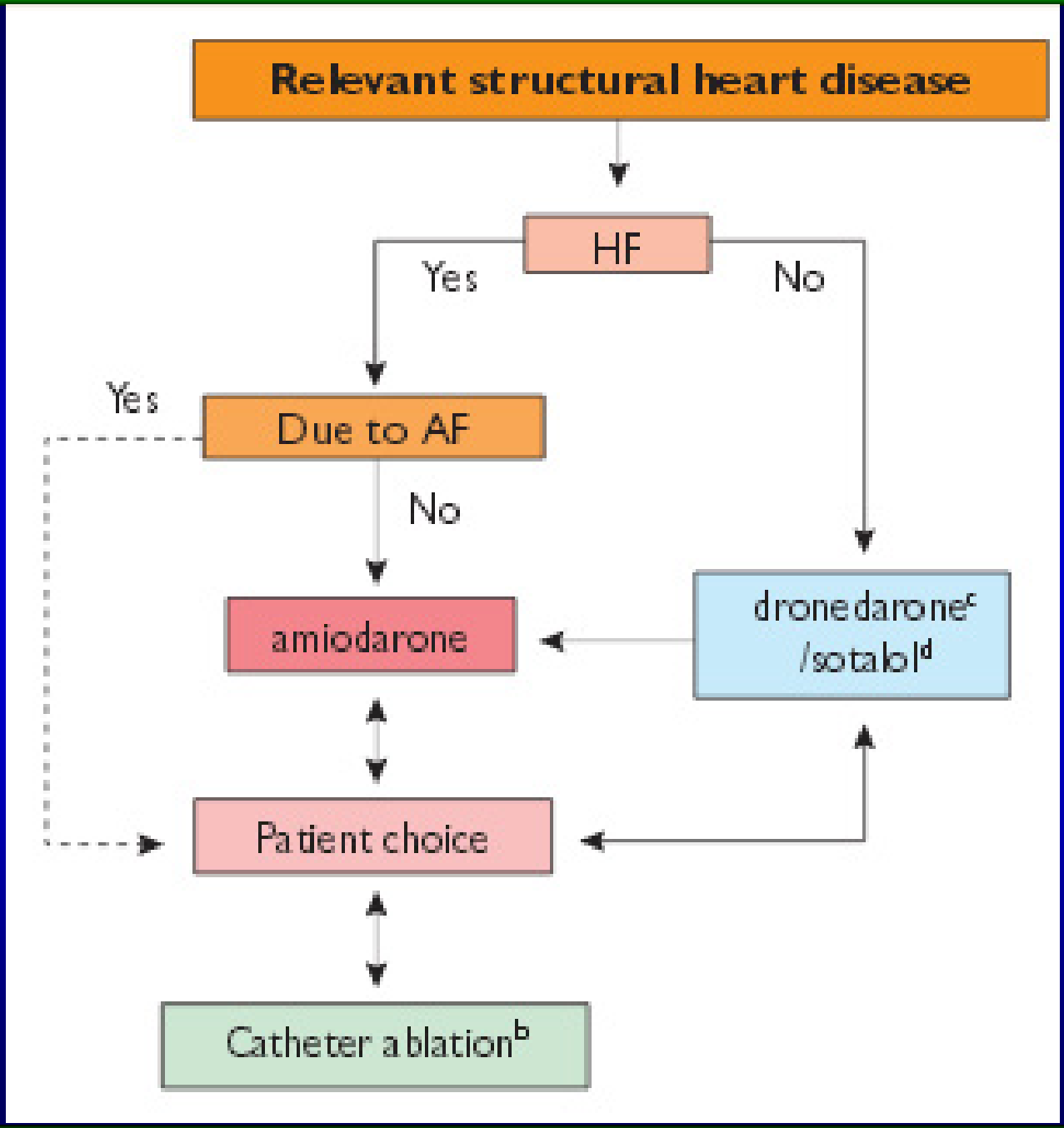
A. Time since first AF diagnosis and risk of AF recurrences




B. Time since first heart failure diagnosis and risk of AF recurrences



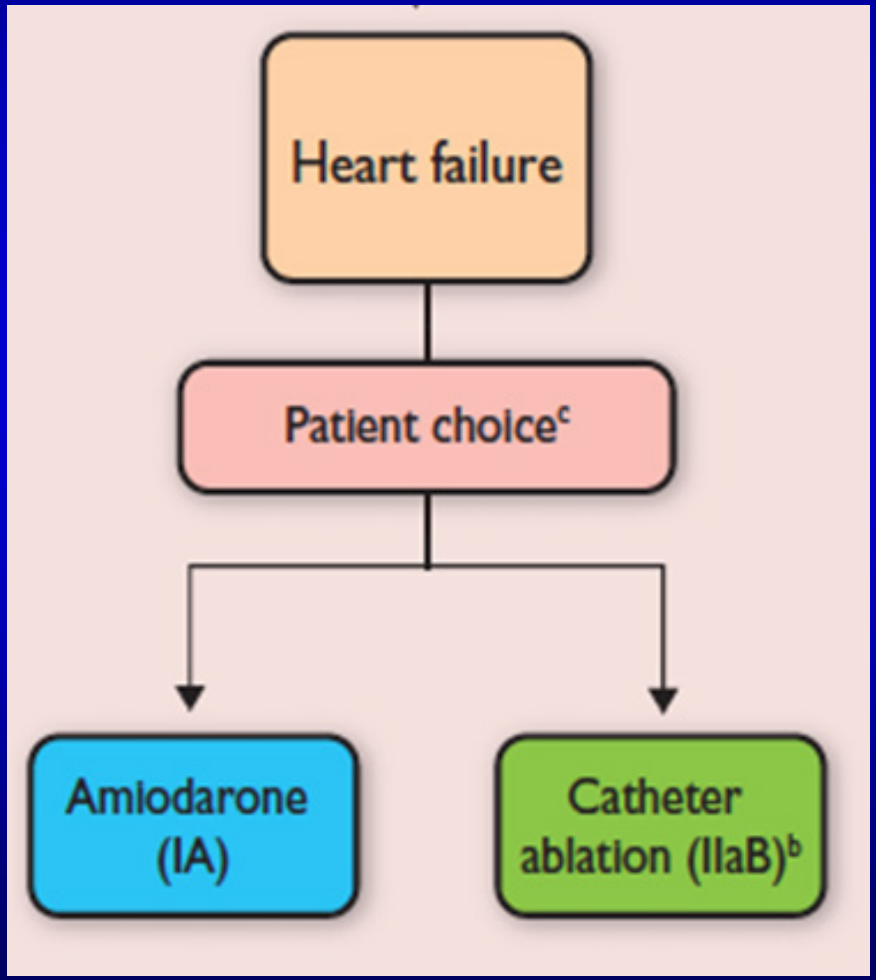

Anselmino M et al. *Circ Arrhythm Electrophysiol* 2014; 7: 1011-1018




Eur Heart J 2012; 33, 2719

# 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

**The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)**




Eur Heart J 2016; Aug 27

# 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

## The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

| | | | |
|---|---|---|---|
| Catheter ablation of symptomatic paroxysmal AF is recommended to improve AF symptoms 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 | 585–587, 713, 727 |
| Ablation of common atrial flutter should be considered to prevent recurrent flutter as part of an AF ablation procedure if documented or occurring during the AF ablation. | IIa | B | 827 |
| Catheter ablation of AF should be considered as first-line therapy to prevent recurrent AF and to improve symptoms in selected patients with symptomatic paroxysmal AF as an alternative to antiarrhythmic drug therapy, considering patient choice, benefit, and risk. | IIa | B | 585 |
| All patients should receive oral anticoagulation for at least 8 weeks after catheter (IIaB) or surgical (IIaC) ablation. | IIa | B C | 727 |
| Anticoagulation for stroke prevention should be continued indefinitely after apparently successful catheter or surgical ablation of AF in patients at high-risk of stroke. | IIa | C | |
| When catheter ablation of AF is planned, continuation of oral anticoagulation with a VKA (IIaB) or NOAC (IIaC) should be considered during the procedure, maintaining effective anticoagulation. | IIb | B C | 760, 768 |
| Catheter ablation should target isolation of the pulmonary veins using radiofrequency ablation or cryothermy balloon catheters. | IIa | B | 585, 715, 716, 734, 735 |
| AF ablation should be considered in symptomatic patients with AF and heart failure with reduced ejection fraction to improve symptoms and cardiac function when tachycardiomyopathy is suspected. | IIa | C | 185, 226–228, 720, 777–779, 828 |
| AF ablation should be considered as a strategy to avoid pacemaker implantation in patients with AF-related bradycardia. | IIa | C | 829, 830 |
| Catheter or surgical ablation should be considered in patients with symptomatic persistent or long-standing persistent AF refractory to AAD therapy to improve symptoms, considering patient choice, benefit and risk, supported by an AF Heart Team. | IIa | C | 468, 735, 777, 831, 832, 1040 |

# In conclusion

**Drug rhythm control strategy (Amiodarone)**
**is to date the first and most used approach**
**but achieves worse results**

**Rhythm control with AF ablation has shown to improve LVEF and quality of life and should be considered the first interventional option (at the early stage)**

**AV node ablation + CRT±D**
**is recommended in case of rhythm control failure**


*Thanks for your attention!*