Atrial Fibrillation:
Rate vs Rhythm Control in Heart Failure

Comparing AFFIRM to AF-CHF

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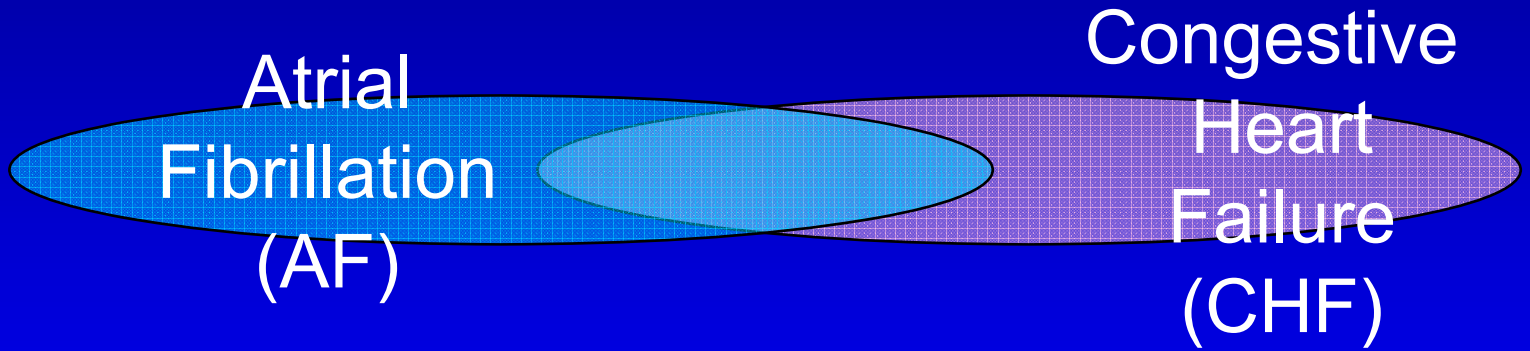
Typical Day at the Office

- 75 yo female, non-ischemic cardiomyopathy
  - NYHA FC III heart failure; EF 0.30; CRT-D
- Recent ICD shocks
- BP: 144/94, P 120, irregular
  - Heart: S1, S2, S3; Lungs: bibasilar rales
- EKG – atrial fibrillation; LBBB (unpaced)

AF in CHF

A Management Challenge

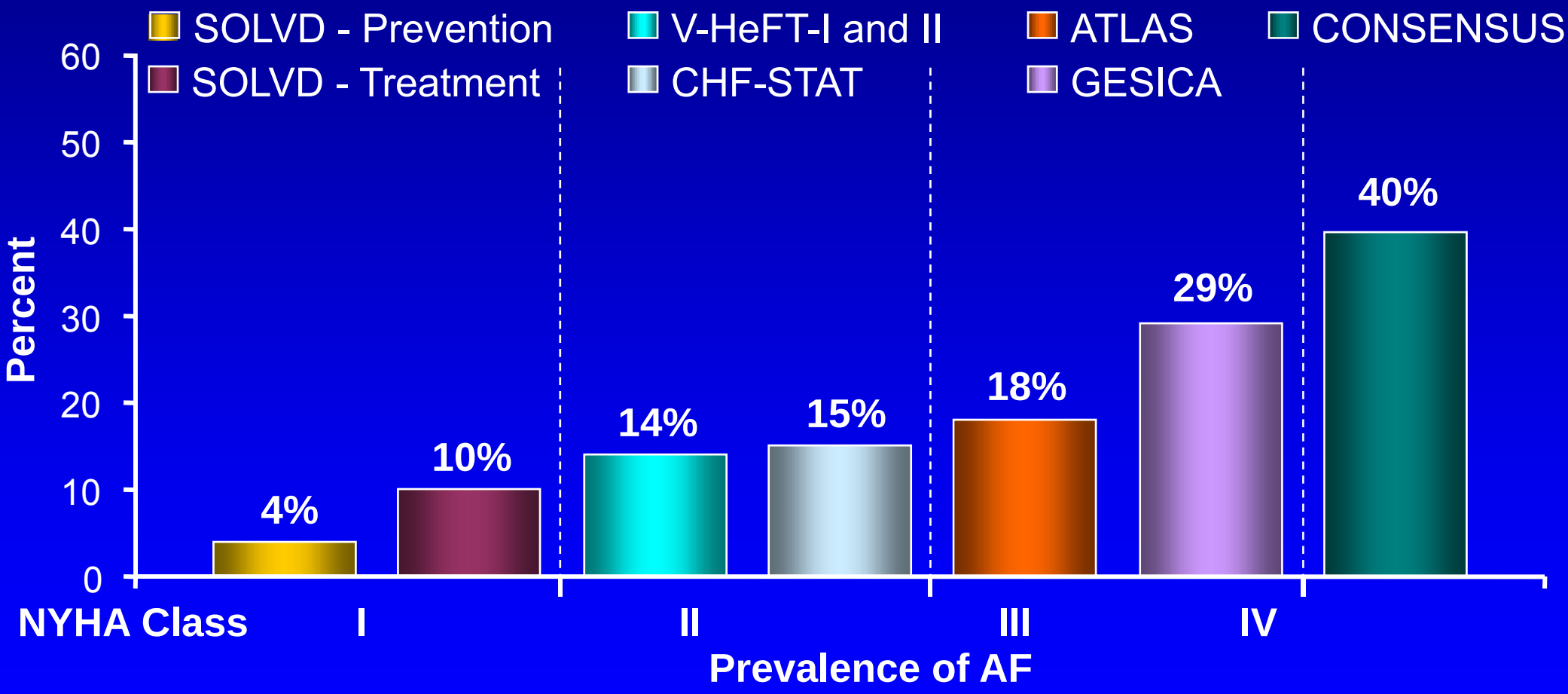
- More advanced heart failure
- Increased risk of death (despite ICD)
- Inappropriate ICD shocks
- Less benefit from CRT (when unpaced)



"Two new epidemics of cardiovascular disease are emerging: atrial fibrillation and congestive heart failure"

Braunwald E. New Engl J Med 1997;337:1360-65

Prevalence of AF - Patients with CHF



Cohn J. N Engl J Med. 1986;314:1547-1552; Cohn J. N Engl J Med. 1991;325:303-310; Doval HC. Lancet. 1994;344:493-498; Johnstone D. Am J Cardiol. 1992;70:894-900; Packer M. Circulation. 1999;100:2312-2318; Singh B. N Engl J Med. 1995;333:77-82; CONSENSUS Trial Study Group. N Engl J Med. 1987;316:1429-1435; Yusuf S. Lancet. 1992;340:1173-1178

The relationship between HF and AF has been examined in several studies over the past 2 decades. Findings from these studies have indicated high rates of AF in patients with HF as well as an association between the severity of HF and the frequency of AF.

The chart above outlines the prevalence of AF in HF study patient populations in a number of trials.

In the Studies of Left Ventricular Dysfunction (SOLVD) Prevention and Treatment Trials, AF was twice as prevalent in the treatment trial as in the prevention trial.

In the Veterans Affairs Vasodilator-Heart Failure Trials (V-HeFT I and II), approximately 14% of patients were being treated for AF. Whereas in the Congestive Heart Failure: Survival Trial of Antiarrhythmic Therapy (CHF-STAT) approximately 15% of patients had AF.

Eighteen percent of patients in the double-blind Assessment of Treatment with Lisinopril And Survival (ATLAS) trial had AF and in an Argentinian study called Grupo de Estudio de la Sobrevida en la Insuficiencia Cardiaca en Argentina (GESICA), approximately 29% of patients had AF.

The Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS) had a much higher percent of the population presenting with AF. In CONSENSUS, approximately 40% of patients in this study had AF.

CHF - Prevalence of AF

Systolic Dysfunction

- AF in 6-10% mild, >40% advanced CHF
- Left ventricular dysfunction increases risk of AF 4.5x in men, 5.9x in women
- AF associated with stroke, clinical deterioration, cardiac events

Owan TE. N Engl J Med 2006;355:251
Olsson LG. J Am Coll Cardiol 2006; 47:1997
Van Veldhuisen DJ. Eur J Heart Fail 2006;8:539
Deedwania PC. Circulation 1998; 98:2575
Erlich JR. J Cardio Electrophysiol 2002;13;399
Benjamin EJ. JAMA 1994;321:840
Pozzoli M. J Am Coll Cardiol 1998; 32:197-204

CHF - Prevalence of AF

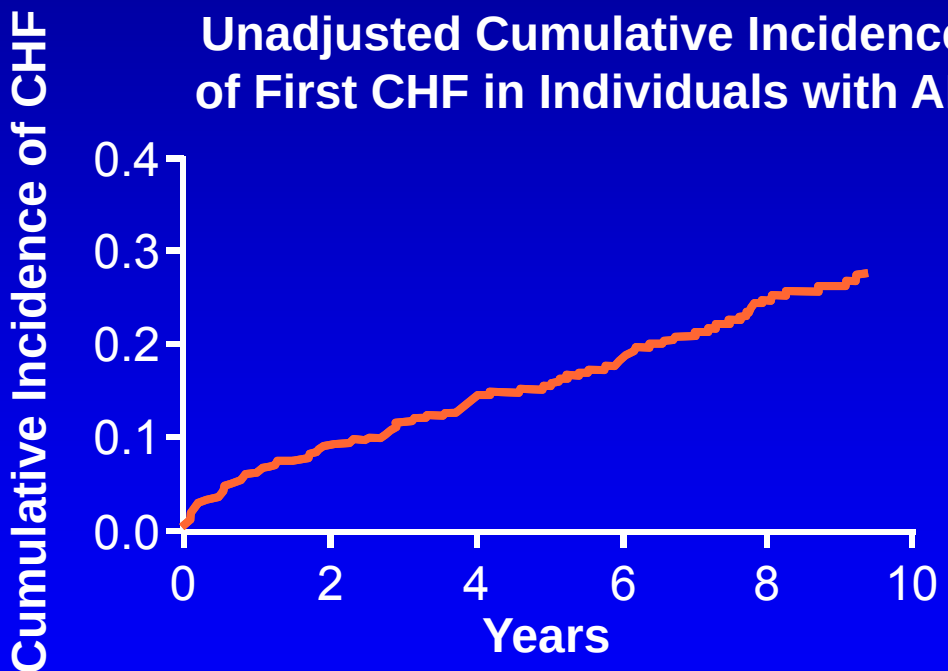
Diastolic Dysfunction

- 10% with abnormal diastolic function have AF after 4 years of follow-up
- 25-30% with new-onset CHF have recent-onset AF with rapid rates
- AF risk proportional to diastolic dysfunction

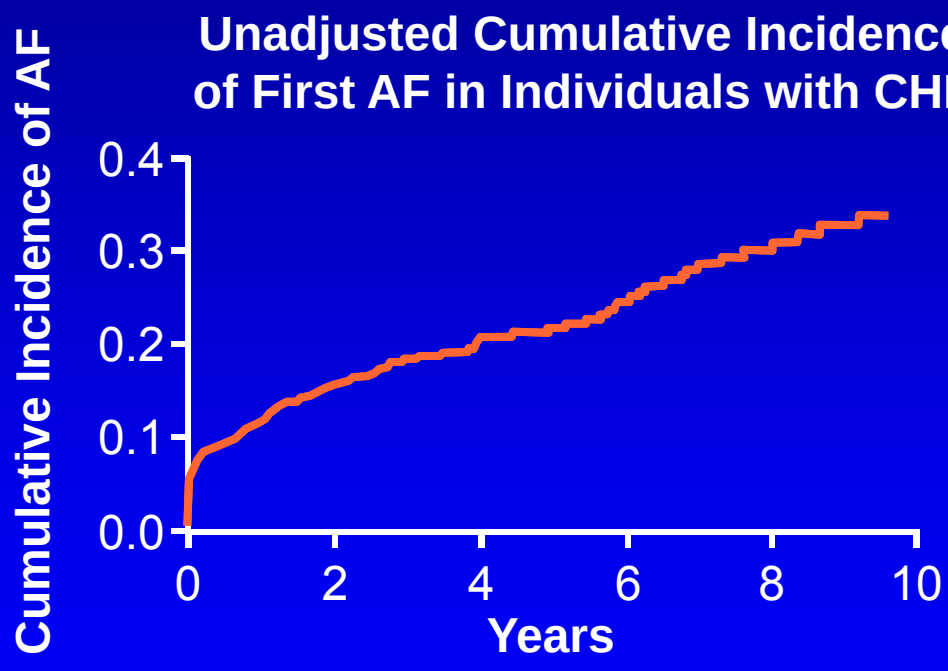
Tsang TS. J Am Coll Cardiol 2002;40:1636
Chen HH. J Card Fail 2002;8:279

Coexistence of AF and CHF

The Framingham Study



921 with AF
26% prior or concurrent CHF
16% developed CHF



931 with CHF
24% prior or concurrent CHF
17% developed CHF

Wang TJ. Circulation 2003;107:2920-5

- Several studies assessing the relationship between AF and HF have resulted in conflicting data most likely due to factors such as focusing on prevalence, varying duration of AF and HF, and differences in population characteristics. Wang et al sought to address these discrepancies by studying participants in the Framingham Study who had new-onset AF or HF from 1948 to 1995. Participants with a history of AF or HF at entry into the study, those who were <50 years old, and those with a first event occurring after 1995 were excluded. HF diagnosis was based on criteria established in the Framingham Study. AF and HF occurring on the same day were deemed concomitant and AF and HF developed during the study were referred to as comorbid conditions. In the first part of the analysis, Wang et al studied the effect of the HF occurrence (in patients who were previously free of HF) on AF survival. The second analysis examined the effect of pre-existing AF and HF on survival.
- One thousand four hundred and seventy patients developed AF, HF, or both between 1948 and 1995. Following the development of AF or HF, the mean follow-up was 5.6 years (5061 person-years) for the AF population and 4.2 years (3823 person-years) for the HF population. Of the 382 patients that developed both AF and HF, 38% developed AF first, 41% HF first, and 21% had both conditions diagnosed on the same day.
- Using multivariable models, the investigators evaluated the effect of HF on mortality in AF patients and vice versa. Restricting the analysis to patients free from HF when diagnosed with AF, development of HF was associated with a hazard ratio for mortality of 2.7 (95% CI, 1.9-3.7) in men and 3.1 (95% CI, 2.2-4.2) in women. They completed a similar assessment of AF on mortality of HF patients. The hazard ratio for mortality for this cohort was 1.6 (95% CI, 1.2-2.1) in men and 2.7 (95% CI, 2.0-3.6) in women.

Mortality with AF and CHF

The Framingham Study

Comorbid Condition as a Time-Dependent Variable

Mortality after AF

Impact of incident HF

Mortality after HF

Impact of incident AF

Comorbid Condition as a Categorical Variable

Mortality after AF

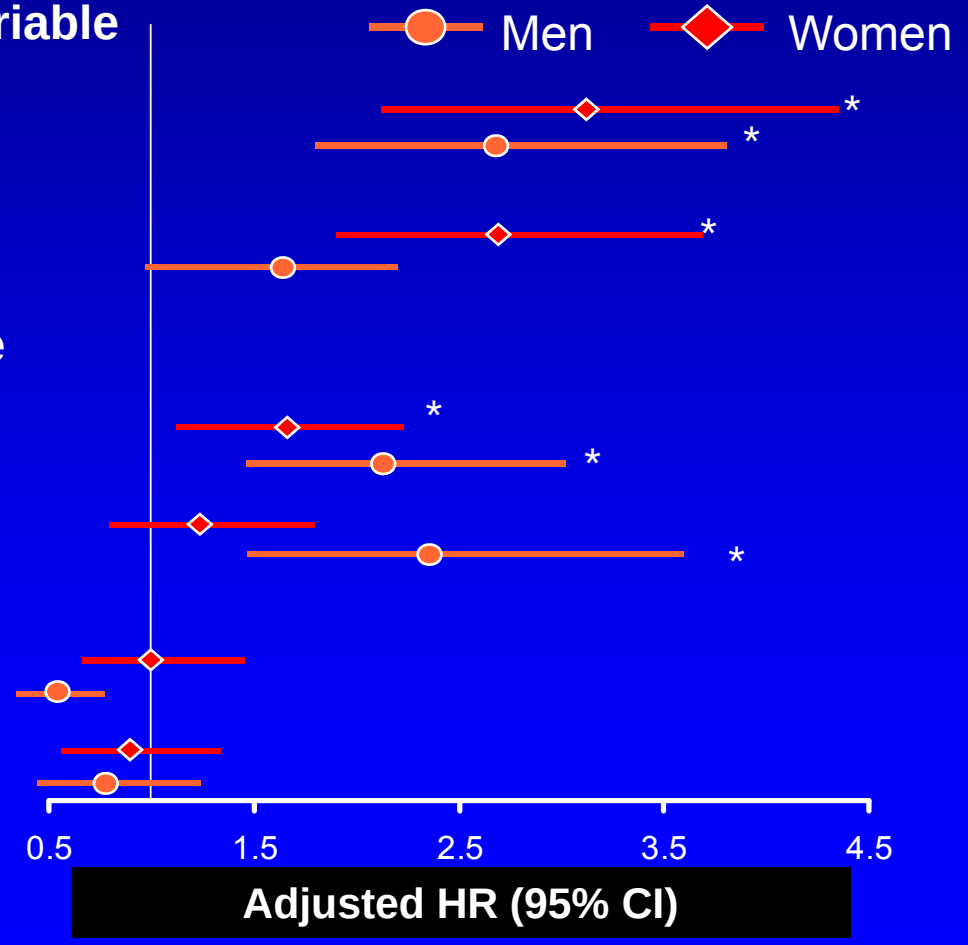
Impact of prior HF

Impact of concurrent HF†

Mortality after HF

Impact of prior AF

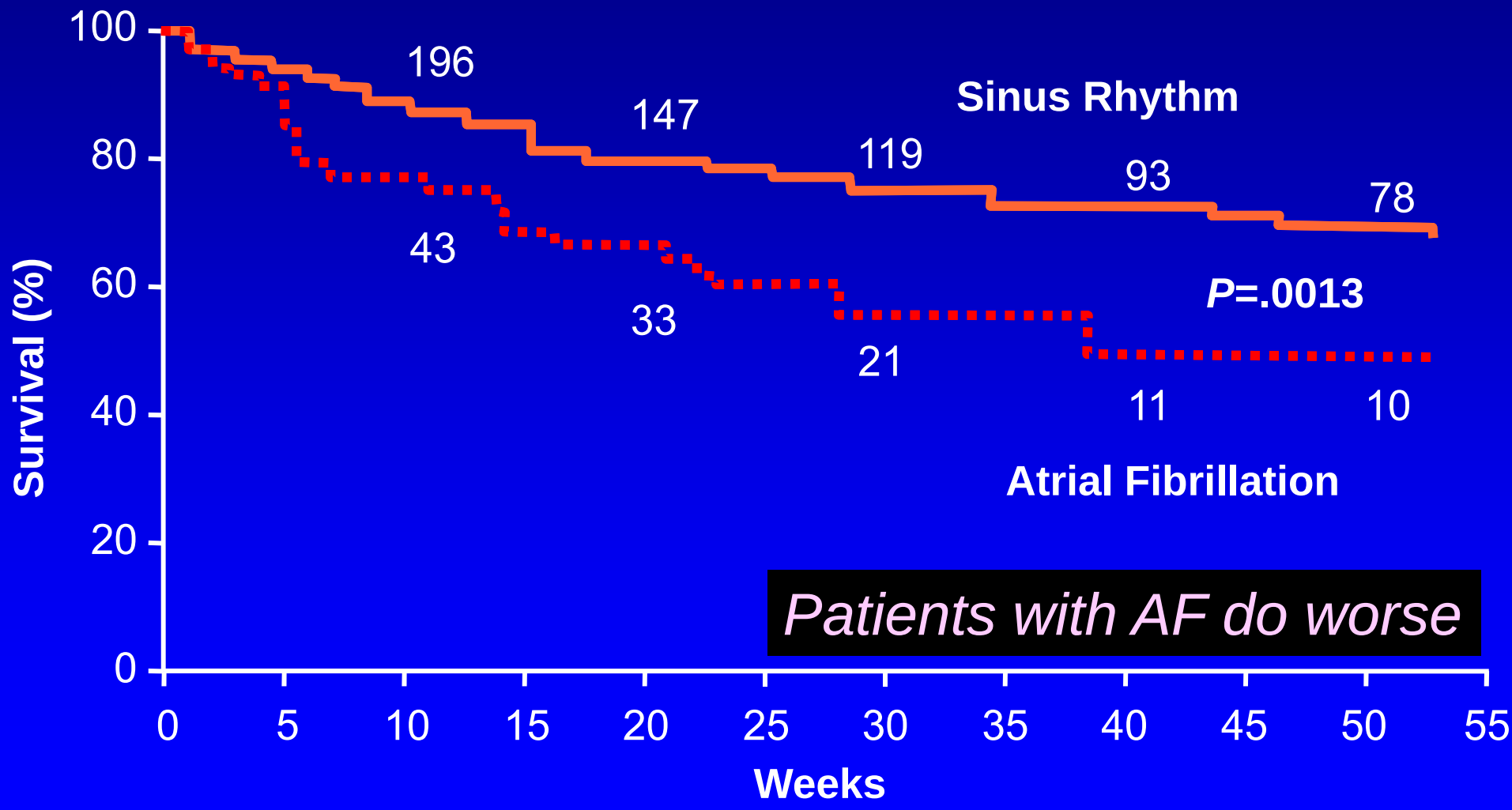
Impact of concurrent AF†



*$P \leq 0.0001$; †Diagnosed on same day

Wang TJ. Circulation. 2003;107:2920-2925

Prognosis in Advanced CHF

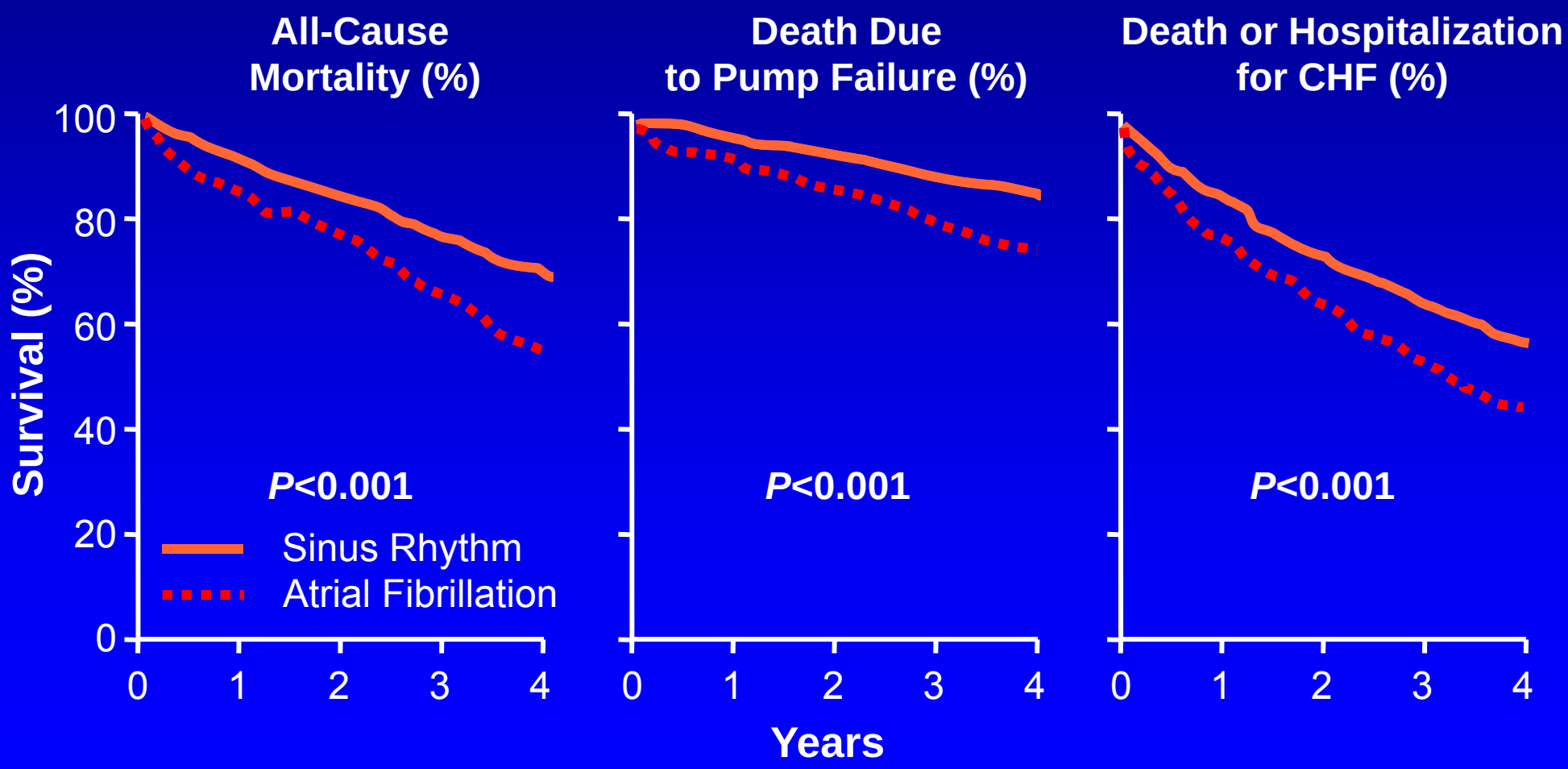


Patients with AF do worse

Middlekauff H. Circulation 1991;84:40-48

- To assess further the prognostic significance of AF in advanced HF, 390 consecutively admitted advanced HF patients (NYHA class III or IV) were followed up for a mean of 236±303 days to evaluate the relation of atrial rhythm to overall survival and sudden death. Mean patient age was 49±12 years. The etiologies of HF were coronary artery disease (177 patients; 45%) and nonischemic cardiomyopathy or valvular heart disease (213 patients; 55%). Patients had a mean LVEF of 0.19±0.07; 19% had paroxysmal (26 patients) or chronic (49 patients) AF.
- HF patients with AF did not differ from those in SR in terms of HF etiology, clinical embolic events, or mean pulmonary capillary wedge pressure on therapy. However, AF patients were more likely to receive warfarin and antiarrhythmic drug therapy. They also had a slightly higher LVEF.
- Ninety-eight patients had died at follow-up (57% experienced sudden death, 36% died of progressive HF). As shown in this slide, overall survival was significantly worse in the AF group compared with the SR group at 1 year (71% vs 52%; *P*=.0013). Additionally, sudden-death-free survival was significantly worse in AF patients (69% vs 82% of SR patients; *P*=.0013). Thus, AF proved to be a marker for increased risk of death in this study, indicating a poorer prognosis for HF patients with AF compared with those in SR.

The SOLVD Trial

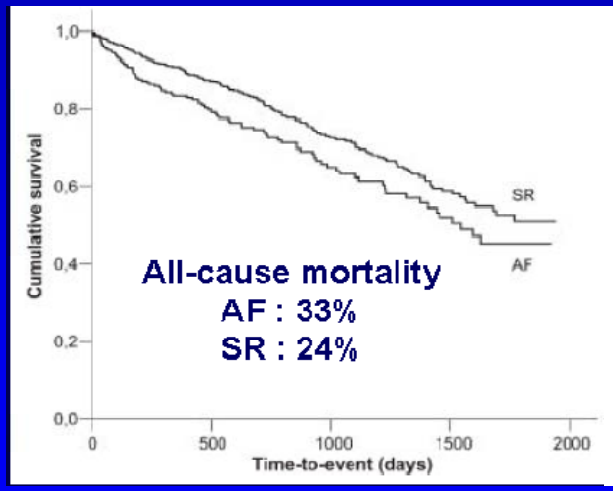


Dries DL. J Am Coll Cardiol 1998;32:695-703

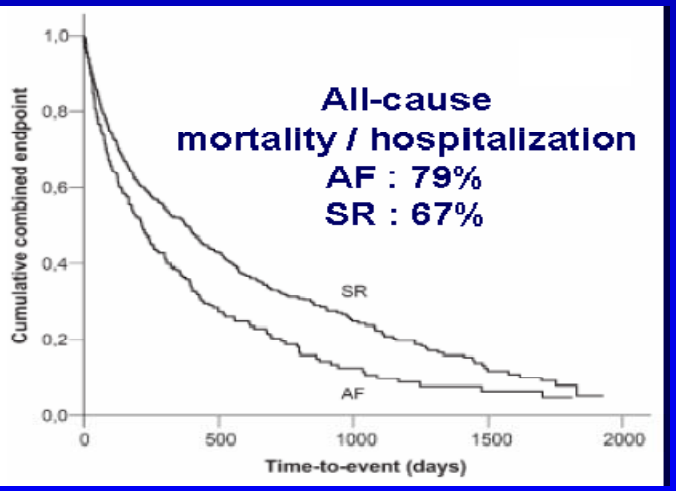
- The effect of AF on the prognosis of HF patients is a topic of ongoing interest. A retrospective analysis was performed on the SOLVD Prevention and Treatment Trials with the goal of determining whether or not the presence of AF in patients with symptomatic or asymptomatic left ventricular dysfunction was associated with increased mortality. Additionally, if an increase in mortality occurred, this analysis hoped to reveal whether or not it was associated with progressive HF or arrhythmic death.
- The HF population of the SOLVD trial (n=4228) was assessed to determine the effect of ACE inhibition therapy on survival. In the prevention arm of the trial (n=4228), most subjects were asymptomatic, NYHA class I patients, but approximately one third were classified as class II patients. The treatment arm included 2569 patients, all of whom had symptomatic HF. Participants of both trials were required to have an LVEF $\leq$35%. All patients were randomized to receive enalapril 2.5 to 20 mg/day or placebo. The primary endpoint of SOLVD was total mortality in both the prevention and treatment groups.

Prognostic Influence of AF in CHF

- 1019 patients with CHF (LVEF ≤0.45)
- 26% AF at baseline; 19% new onset AF



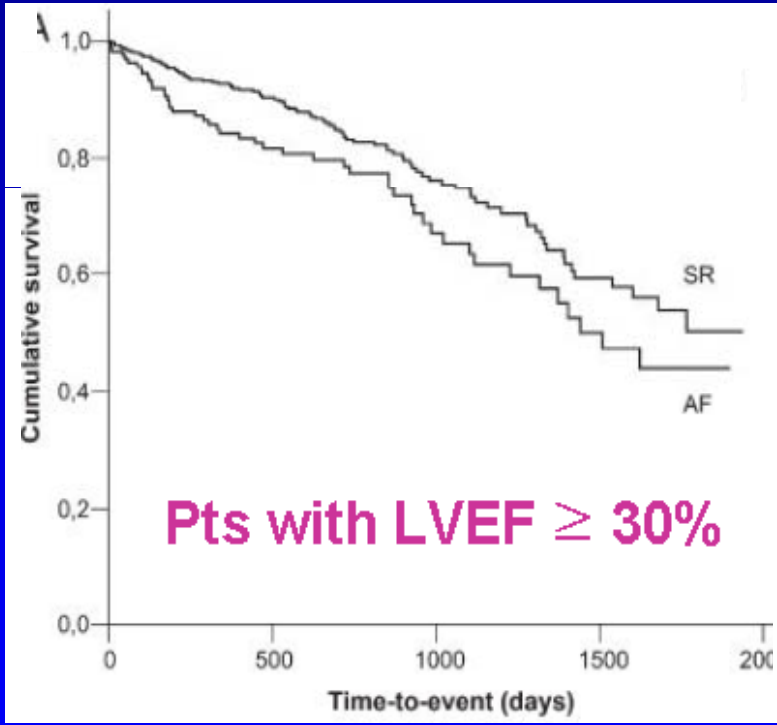
HR for death in AF patients
1.38 (CI: 1.07 – 1.78, p=0.01)



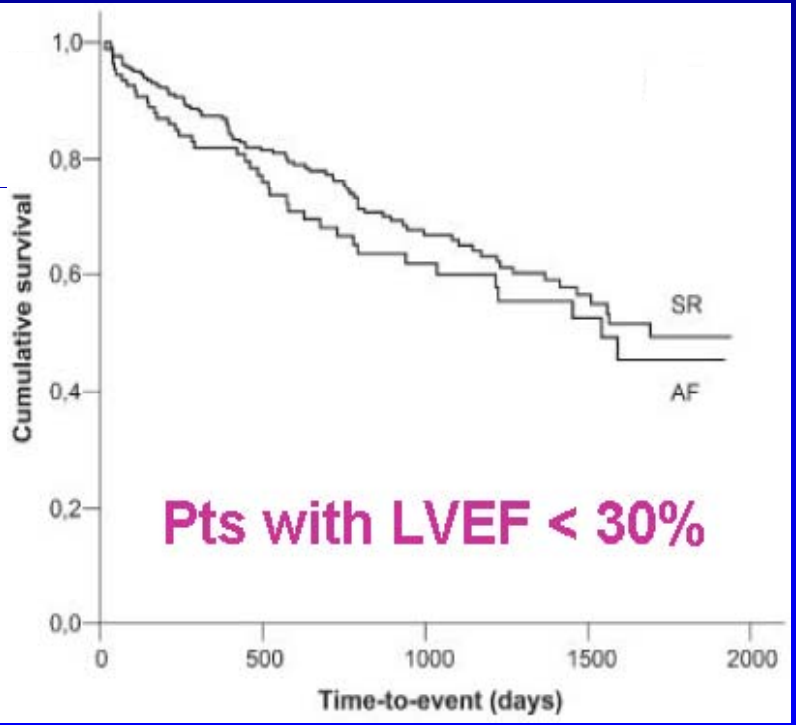
HR = 1.43
(CI: 1.22 – 1.68, p<0.001)

Corell P. Eur J Heart Fail 2007;9:258

AF Prognostic if LVEF ≥ 30%



Baseline AF - increased mortality
HR 1.46; CI 1.04-2.07; p=0.03

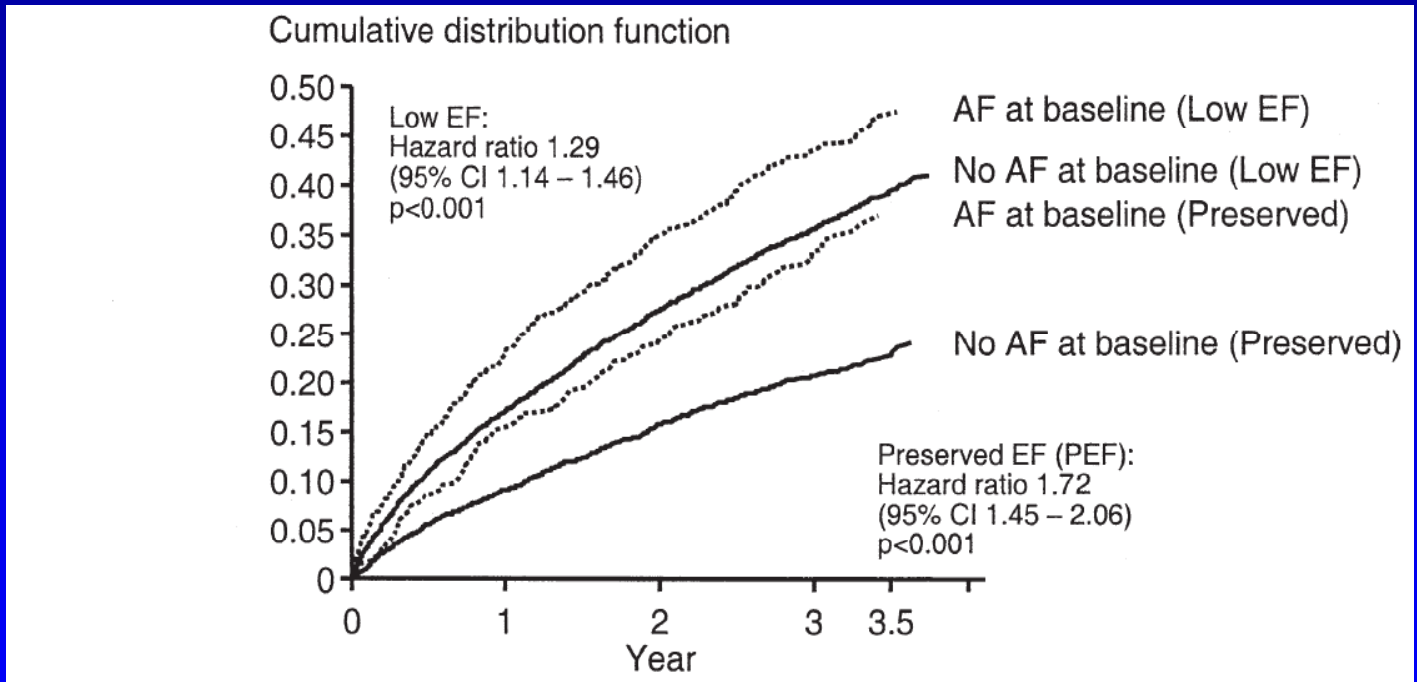


Baseline AF – same mortality
HR 1.24; CI 0.85-1.80; p=0.27

Corell P. Eur J Heart Fail 2007;9:258

The CHARM Trial

AF Prognostic Despite LVEF



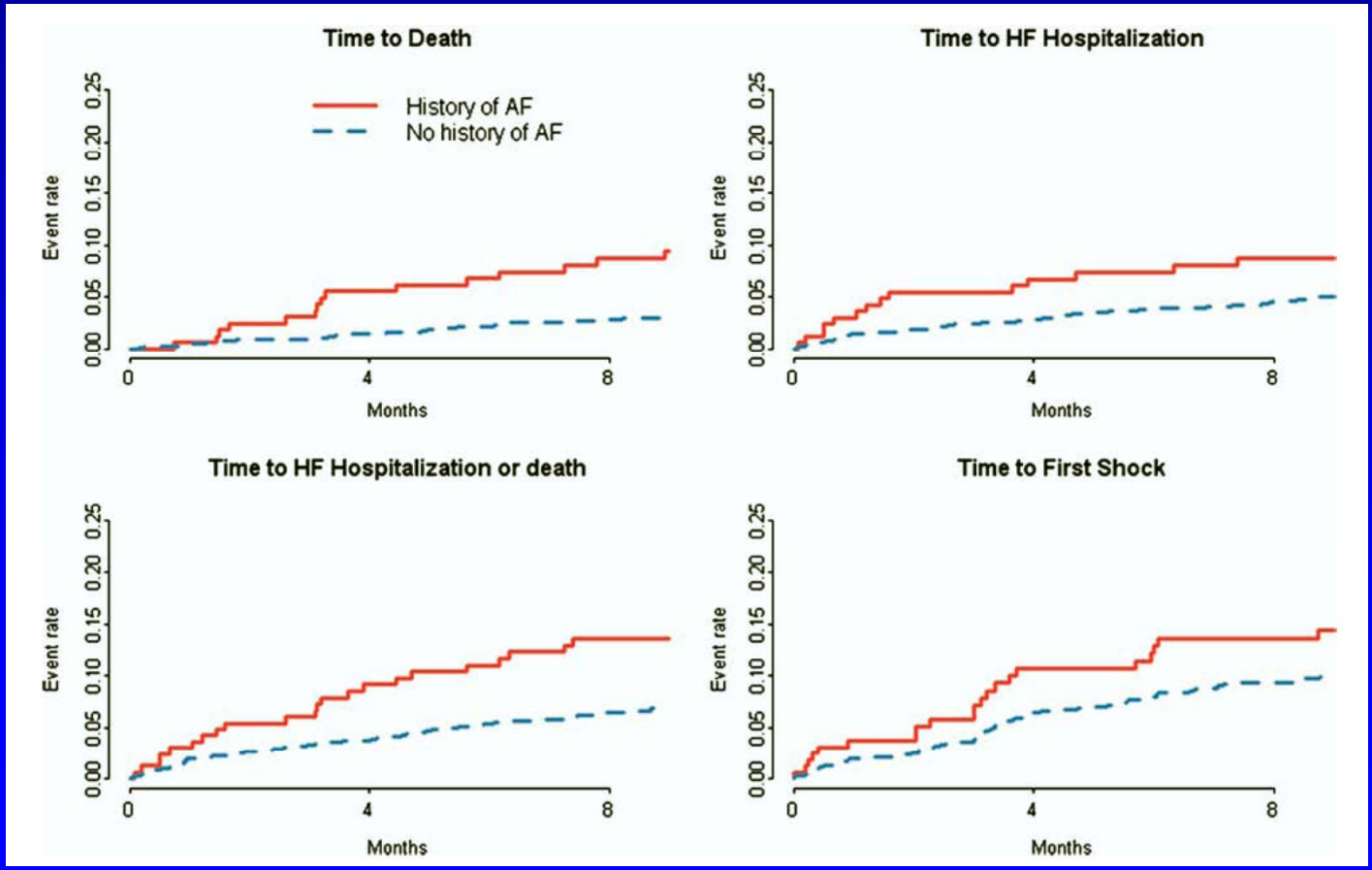
Number at risk

No AF & Low EF	3906	3207	2755	1963
No AF & PEF	2545	2294	2096	1276
AF & Low EF	670	509	417	289
AF & PEF	478	399	353	203

Olsson LG. J Am Coll Cardiol 2006;47:1997–2004

INTRINSIC RV Trial

AF Identified Risk

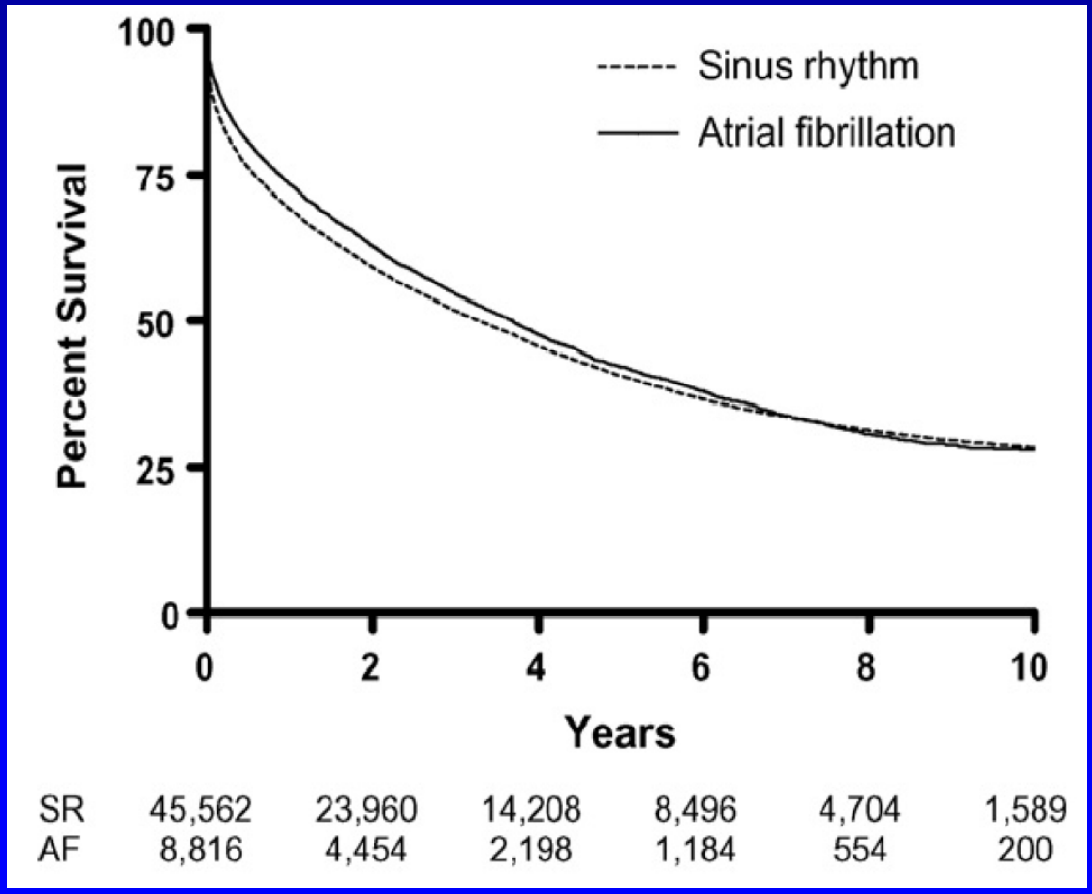


p<0.01 unadjusted model

Bunch T. Heart Rhythm 2009;6:2-8

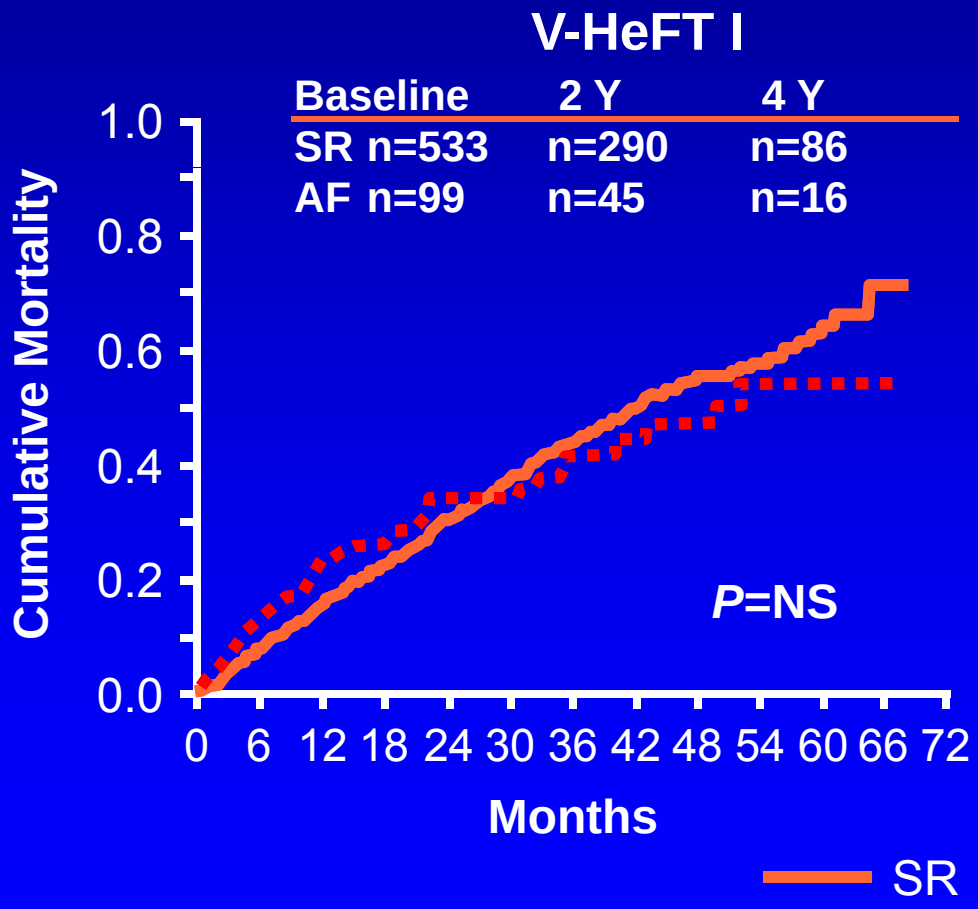
AF in CHF - Not Prognostic

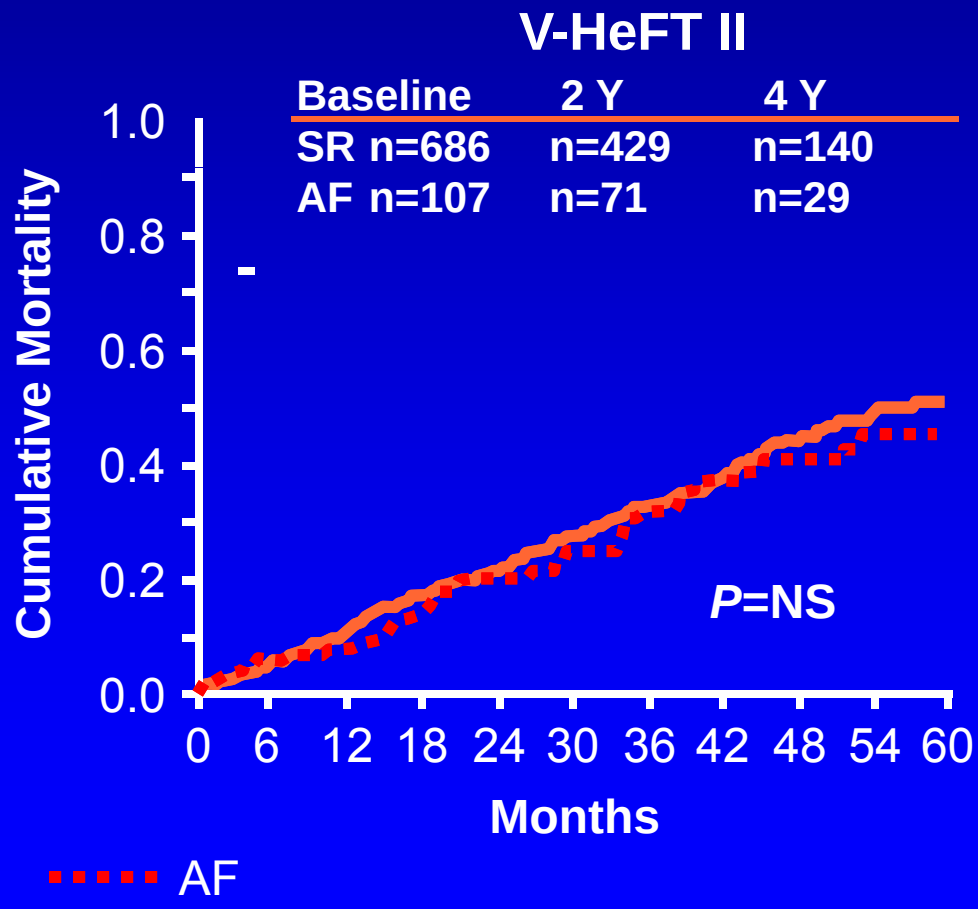
55,106 Admissions - CHF in New Zealand



Wasywich CA. Heart Lung Circ 2006;15:353

AF in CHF - Not Prognostic





SR AF

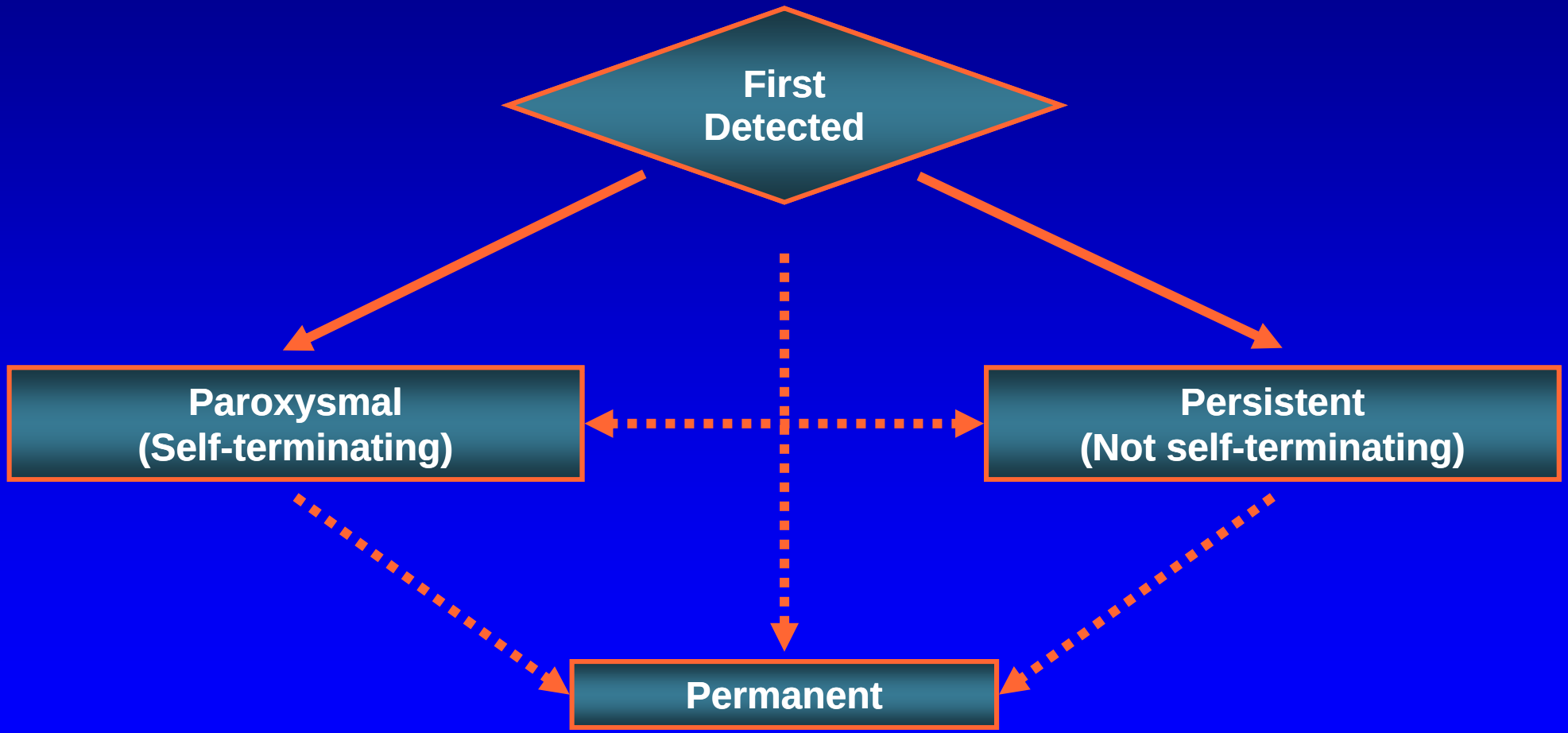
Carson P. Circulation 1993;84 (suppl VI):VI-102–VI-110

- In an effort to evaluate the impact of AF in patients with mild to moderate HF, the relation of AF seen on first Holter monitor to morbidity and mortality was studied in 632 patients in the V-HeFT I and 795 patients in the V-HeFT II. Ninety-nine patients (16%) and 107 patients (13%) had baseline AF on Holter monitor in the 2 trials, respectively.
- All V-HeFT I patients continued to take digoxin and a diuretic and were further relegated to receive 1 of 3 double-blinded regimens: placebo, full-dose prazosin (20 mg/day), or full-dose hydralazine 300 mg/day and isosorbide dinitrate 160 mg/day. Patients in the V-HeFT II trial comprised 121 patients not in the hydralazine-isosorbide arm in V-HeFT I. These patients were randomly assigned to receive either enalapril 20 mg/day or hydralazine 300 mg/day with isosorbide 160 mg/day.
- V-HeFT I included male patients aged 18 to 75 years with chronic mild to moderate HF. The 99 AF patients in this group were older (mean 59.9 vs 58.2 years) and fewer had CAD (25.3% vs 47.7%) compared with the patients in SR. In addition, AF patients showed smaller echocardiographic systolic and diastolic ventricular dimensions, and had larger left atrial size and a greater cardiothoracic (CT) ratio. In addition, AF patients had generally lower peak exercise oxygen consumption compared with those in SR (14.1 vs 14.9 mL/kg/min).
- V-HeFT II also enrolled male chronic HF patients between the ages of 18 and 74 years. At baseline, the 107 patients with concomitant AF had a higher EF (31.8%) compared with non-AF patients (28.7%). AF patients tended to have smaller left ventricular systolic and diastolic volumes, but left atrial size and CT ratios were higher, as in V-HeFT I.

Why Difference Between Studies?

- Maybe differences in AF types are present
- Maybe rate control is important

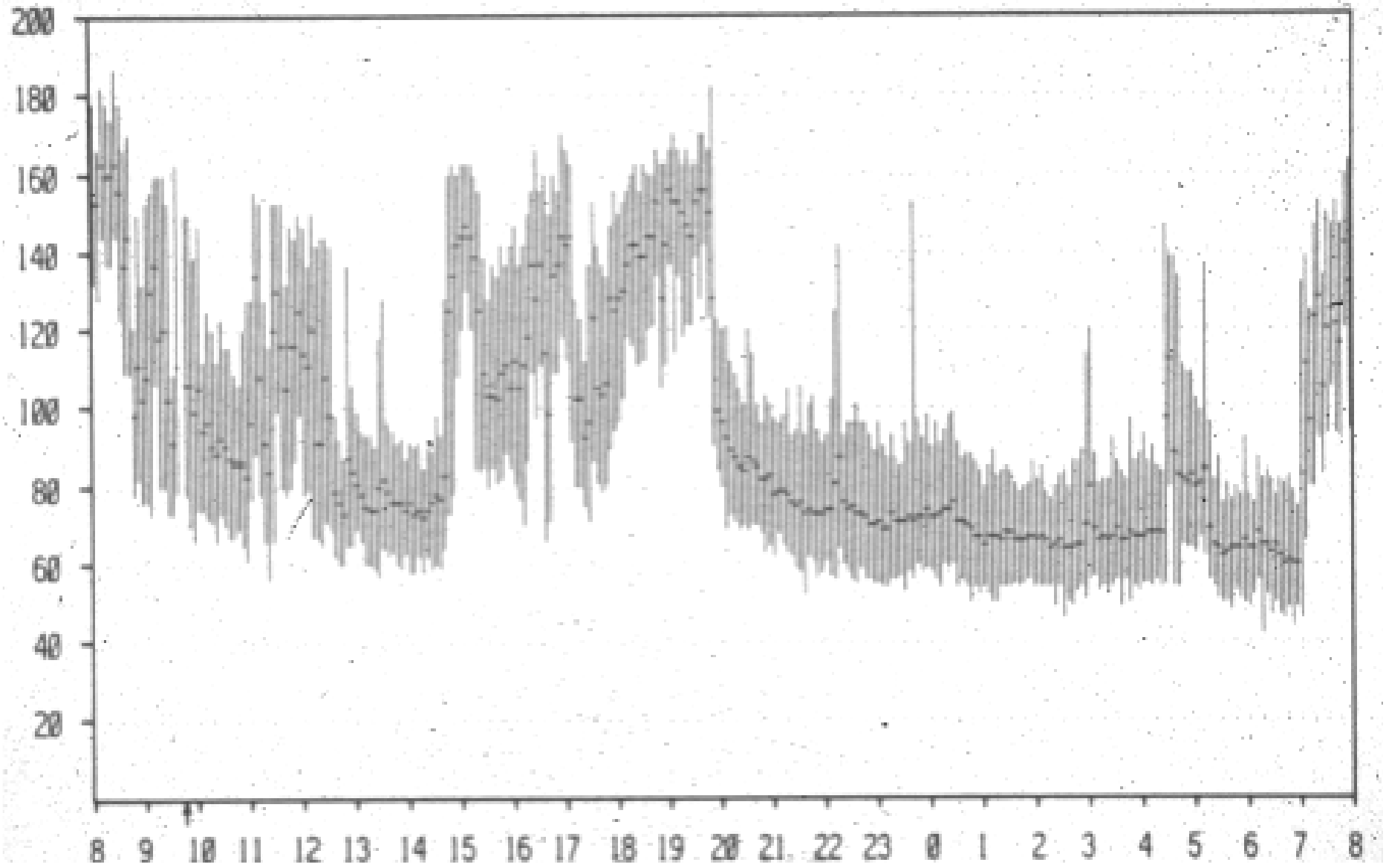
Management Depends on AF Type



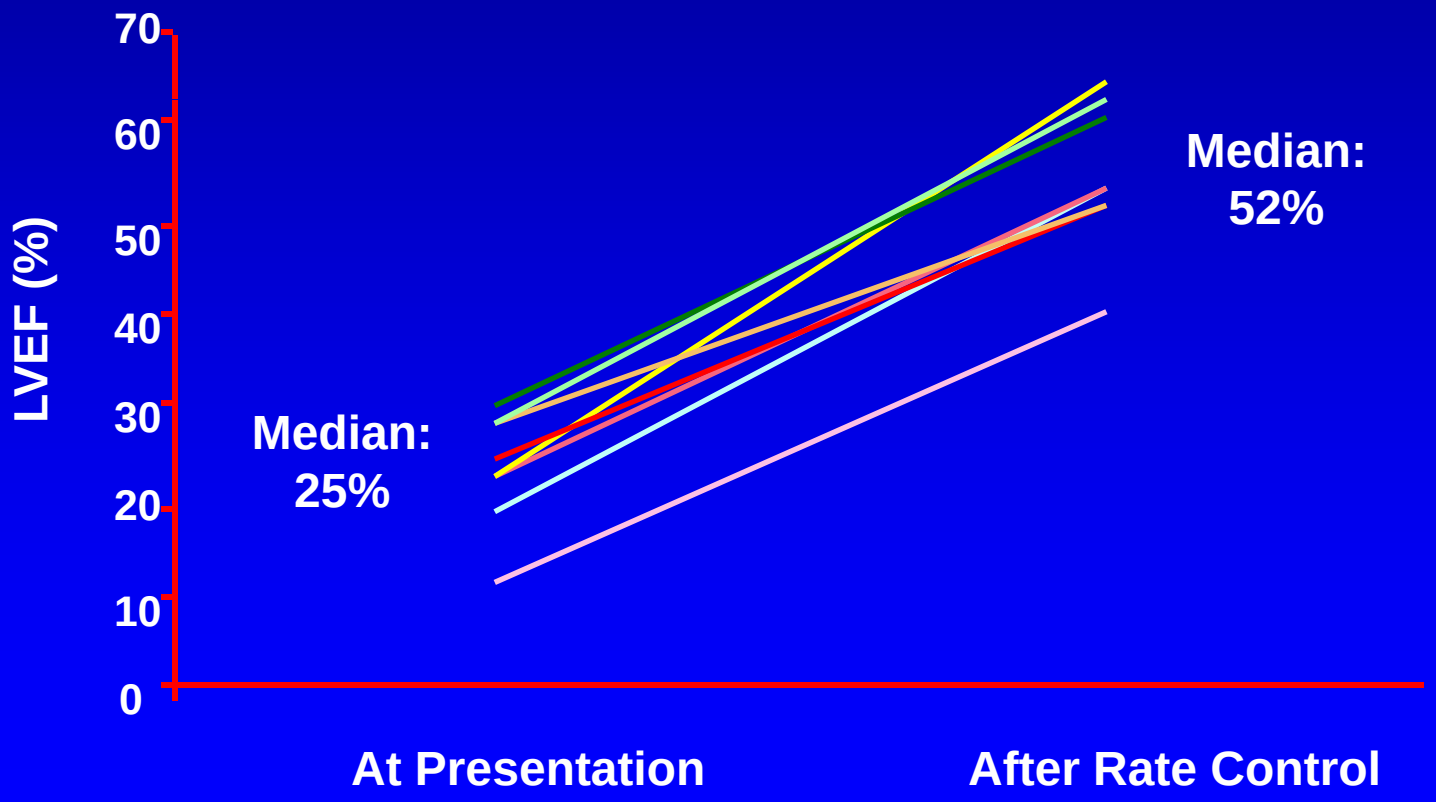
ACC/AHA/ESC Guidelines

Fuster V. Circulation 2006;114:700-752

AF – Rapid, Inappropriate and Irregular Rate



Rate Control in AF: Improved LVEF



Grogan M. Am J Cardiol 1992;69;1570-1573

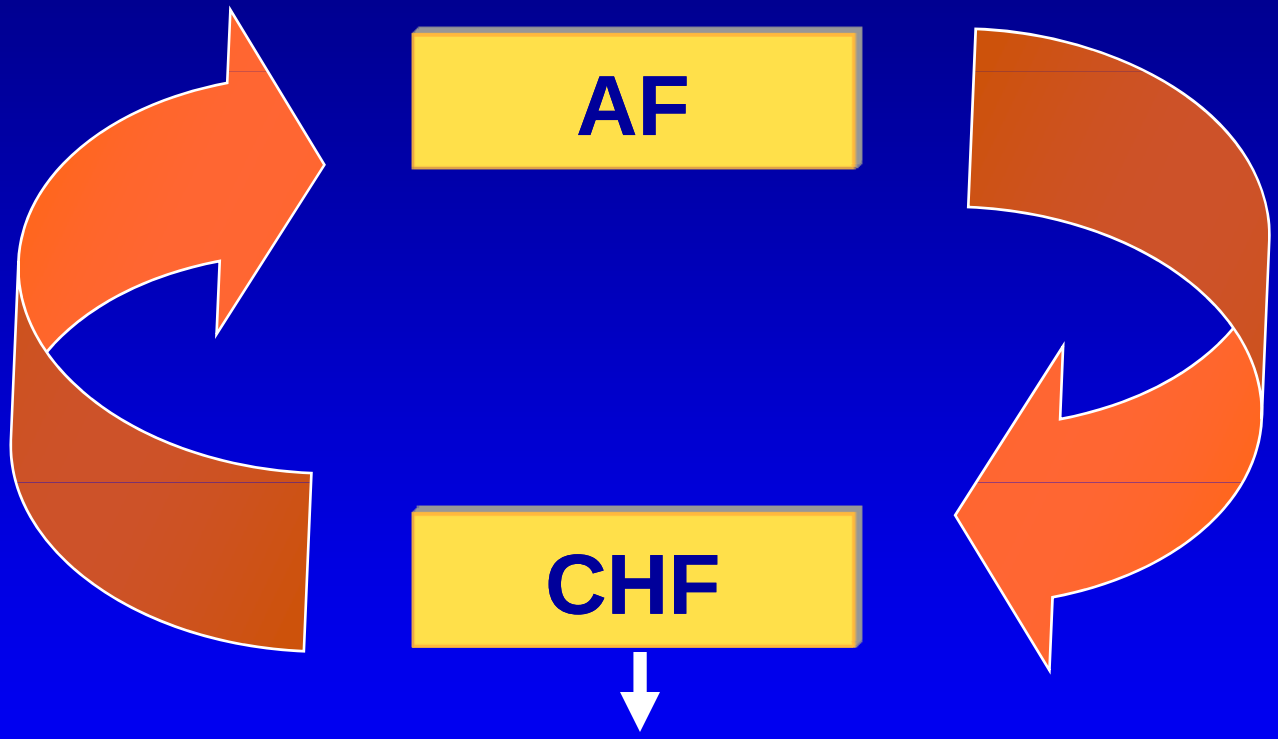
Tachycardia-Mediated Cardiomyopathy

AF - most common cause

- 24 patients with NYHA Class III or IV CHF, LVEF = 0.26 ± 0.09
- With rate or rhythm control, LVEF improved to 0.51 ± 0.05
- After LVEF improved, rapid decline with recurrent tachycardia and risk of sudden death

Nerheim P. Circulation 2004;110:247-252

A Vicious Cycle



Worsening symptoms
Increased mortality

Maisel WH. Am J Cardiol. 2003;91:2D-8D

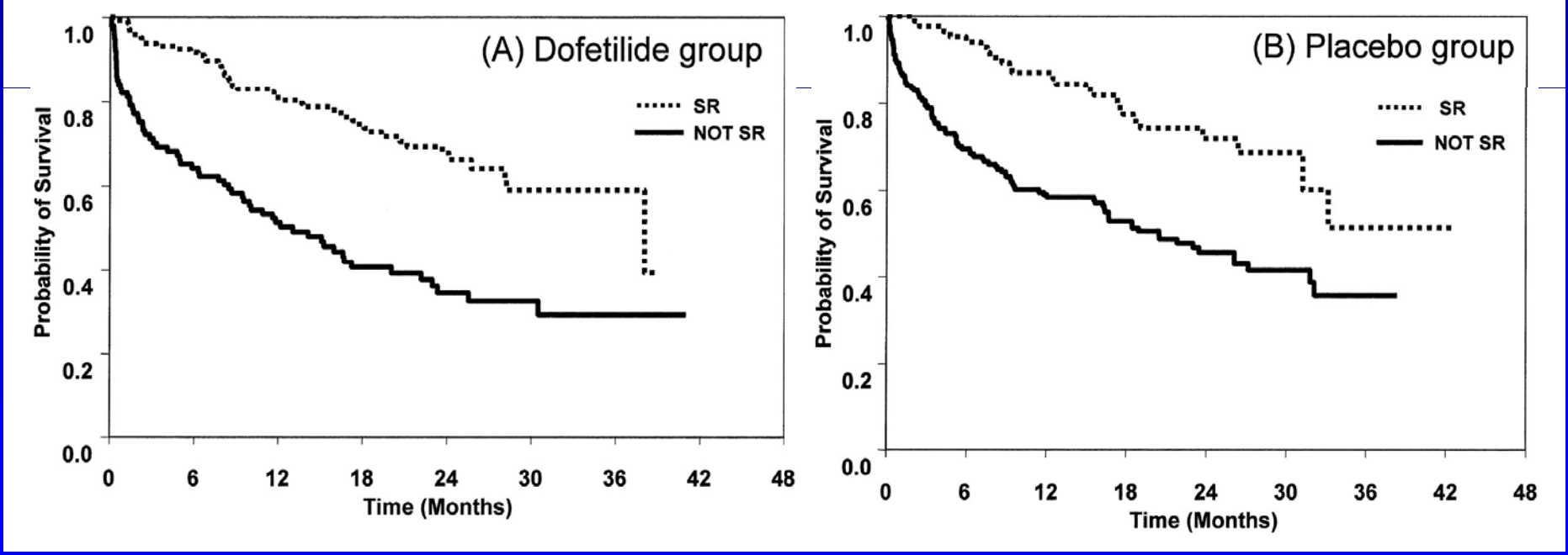
- The pathophysiologic changes that take place in patients who have both AF and heart failure (HF) are extremely complex and are not well understood. AF prevalence increases with the severity of HF. For example, AF has been observed to occur in ≤5% of patients with asymptomatic or minimally symptomatic HF (NYHA class I symptoms) and in nearly 50% of patients with NYHA class IV symptoms. Thus, it appears that pathophysiologic changes in electrophysiologic parameters, neurohormonal activation, and mechanical components combine to form a reciprocal environment in which HF predisposes to AF and AF exacerbates HF.
- A significant body of evidence suggests that HF produces changes in the atrium that make it more vulnerable to the development of and maintenance of AF. Morphologic, hemodynamic, and neurohormonal alterations, as well as cellular and extracellular remodeling result in conduction heterogeneity. HF may also beget AF by altering atrial refractoriness because of the stretching of cardiac tissue. Interstitial fibrosis resulting from HF-related activation of the renin-angiotensin-aldosterone system causes increased production of angiotensin II, which may lead to heterogeneous changes in atrial repolarization from areas of slow conduction. This substrate is known to predispose to the development of AF.

Is Rhythm Control Important?

Yes and No

DIAMOND Trial – Post Hoc Analysis

Sinus Rhythm - Improved Outcomes

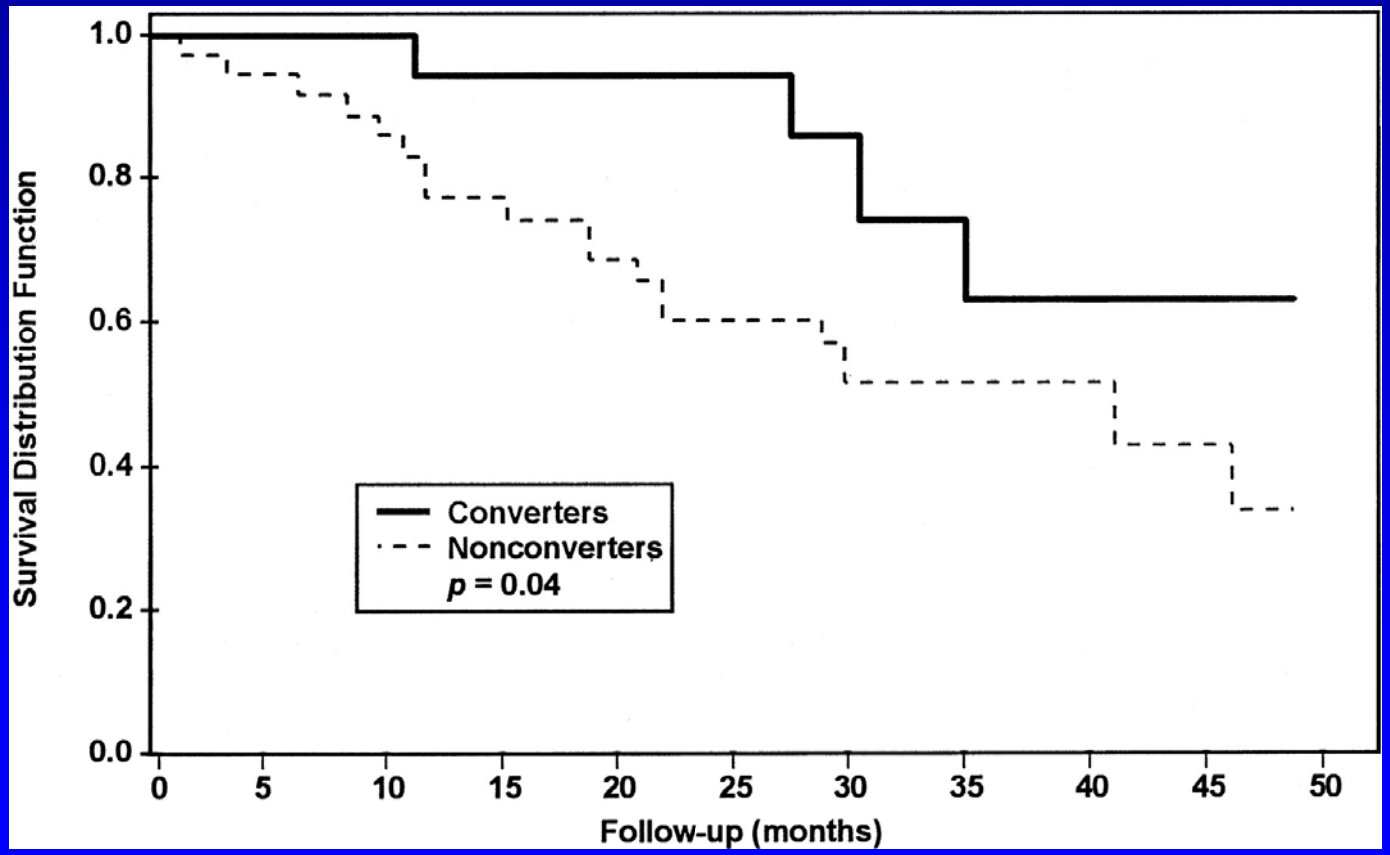


Sinus and Mortality (multivariate analysis)
RR 0.44 (0.30-0.64); P<0.0001

Pedersen OD. Circulation 2001;104:292-6

CHF-STAT – Post Hoc Analysis

Amiodarone Converters Do Better



Deedwania PC. Circulation 1998;98:2574-9

Rhythm vs Rate Control in AF

6 Prospective, Controlled, Randomized Trials

- PIAF — Pharmacological Intervention in Atrial Fibrillation (pilot)
- STAF — STrategies in Atrial Fibrillation (pilot)
- AFFIRM — Atrial Fibrillation Follow-up Investigation of Rhythm Management
- RACE — RAte Control versus Electrical Cardioversion for Persistent Atrial Fibrillation
- SAFE-T — Sotalol and Amiodarone For Effectiveness Trial
- HOTCAFÉ — How to Treat Chronic Atrial Fibrillation Efficacy

AFFIRM Trial

Rhythm vs Rate Strategy to Treat AF

- 4060 patients - 65 yo or risk factor for stroke
- Long-term treatment thought necessary
- No contraindication to anticoagulation
- Rhythm or rate strategy possible
- Endpoint - mortality

AFFIRM Investigators. N Engl J Med 2002;347:1825-33

AFFIRM Trial

Treatment groups

- Rhythm control
  - Antiarrhythmic drug chosen by physician
  - Electrical cardioversion as necessary
- Rate control
  - β-blocker, Ca^{2+} channel blocker, digoxin or combinations
  - Target heart rate ≤ 80 bpm at rest and ≤ 110 bpm with 6-minute walk or 24 hour Holter with rate ≤ 100 bpm and no heart rate > 100% maximum predicted age-adjusted rate

AFFIRM Investigators. N Engl J Med 2002;347:1825-33

AFFIRM Trial

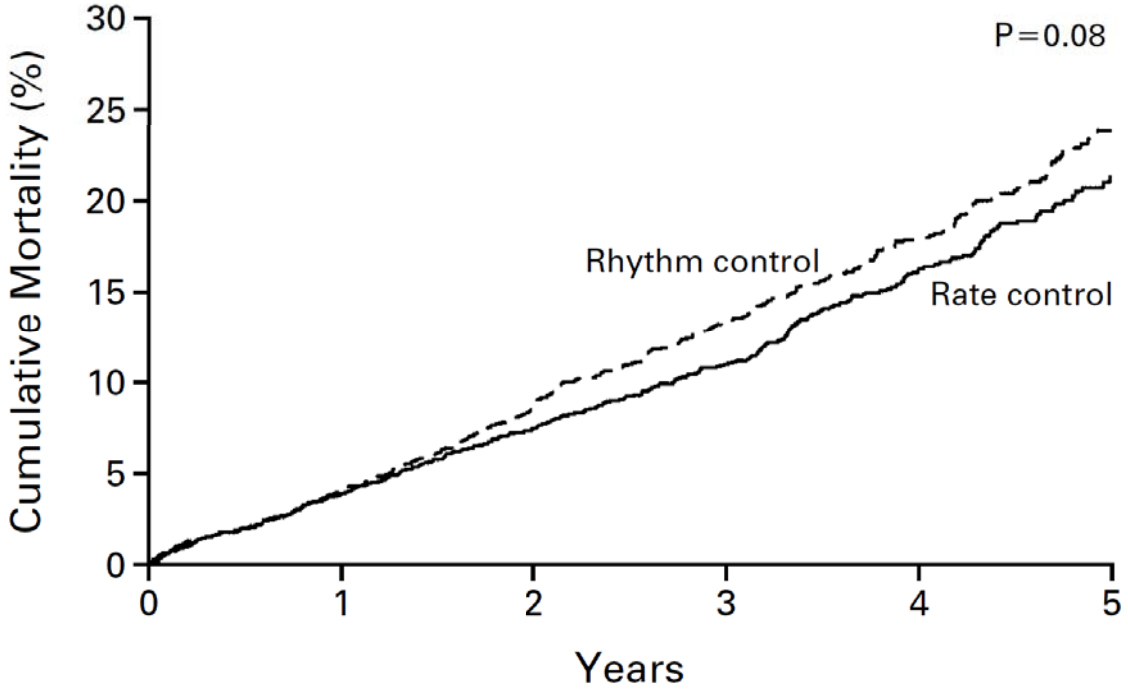
Baseline characteristics

- Mostly men
- Age 69±9
- 70% had hypertension
- 23% with heart failure
- LVEF mean 54.7±13.5%

AFFIRM Investigators. N Engl J Med 2002;347:1825-33

AFFIRM Trial

No Difference in Mortality



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)

AFFIRM Investigators. N Engl J Med 2002;347:1825-33

Rhythm Control - AFFIRM Trial

More Adverse Events

- More ventricular tachycardia (0.8% vs 0.2%, p=0.007)
- More PEA, bradycardia or rhythm requiring resuscitation (0.6% vs <0.1%, p=0.01)
- More hospitalizations (80% vs 73%, p<0.001)
- More discontinued drugs
  - Pulmonary or GI events, prolonged QT, other (p<0.001)
  - Bradycardia (p=0.001)

AFFIRM Investigators. N Engl J Med 2002;347:1825-33

AFFIRM Trial - Crossovers

- 594 switched from rhythm to rate control due to inability to maintain sinus and drug intolerance
- 248 switched from rate to rhythm control, usually due to AF symptoms or heart failure
- At one, three and five years, more crossed over from rhythm control ($p<0.001$)

AFFIRM Investigators. N Engl J Med 2002;347:1825-33

AFFIRM - Implications

- No difference in mortality for those receiving either rhythm or rate control for AF
- More hospitalizations and adverse events in the rhythm control group

AFFIRM - Implications

- No difference in mortality for those receiving either rhythm or rate control for AF
- More hospitalizations and adverse events in the rhythm control group

Rate control is a reasonable strategy for AF patients

AFFIRM Trial

Risk of Death Higher with Rhythm Control

- Age ≥65
- Coronary artery disease
- No congestive heart failure

Rate control acceptable in enrolled patients

AFFIRM Investigators. N Engl J Med 2002;347:1825-33

AFFIRM Trial

Risk of Death Higher with Rhythm Control

- Age ≥65
- Coronary artery disease
- No congestive heart failure

Rate control acceptable in enrolled patients

What about patients with CHF?

AFFIRM Investigators. N Engl J Med 2002;347:1825-33

AF-CHF Trial

Does Rhythm Control Improve Outcome?

- 1376 patients, 123 international sites
- LVEF ≤0.35, NYHA class II-IV, CHF hospitalization in last 6 mos or LVEF ≤0.25
- Excluded
  - AF > 12 months or AF with reversible cause
  - CHF with reversible cause
  - Decompensated CHF

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

AF-CHF Trial

Treatment groups

- Rhythm control – cardioversion and drug (amiodarone, sotalol, dofetilide)
- Rate control - < 80 bpm at rest and < 110 bpm with 6-minute walk
  - Adjusted dose β-blocker ± digoxin
  - AV node ablation and pacemaker if target not met

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

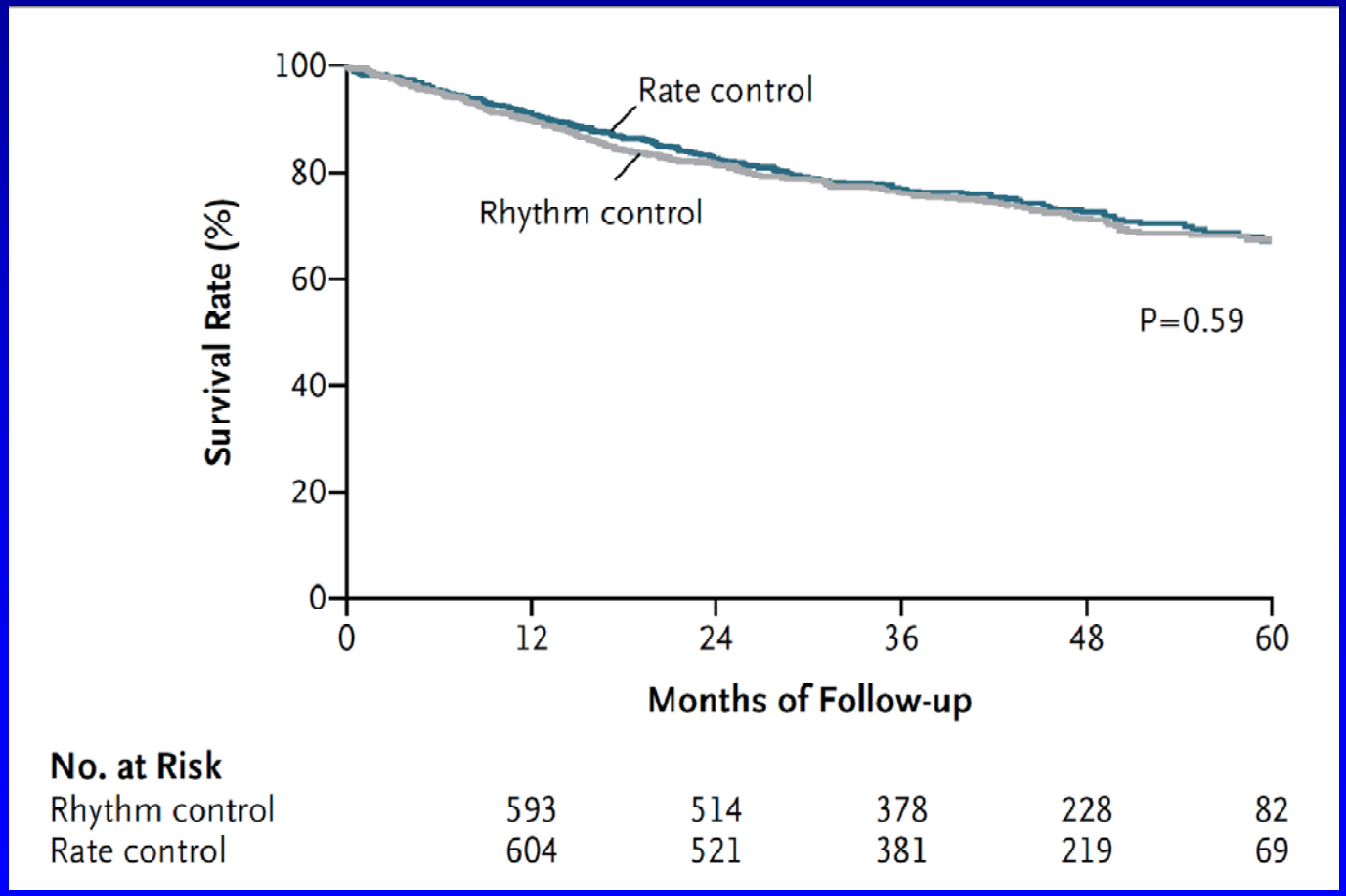
AF-CHF Trial

Baseline Characteristics

- Mostly men; mean age = 67
- Nearly 50% had coronary artery disease
- Mean LVEF = 27 ± 6%
- 1/3 NYHA class III/IV at enrollment, 3/4 in prior 6 mos
- 2/3 had persistent AF
- Participants took digoxin, β-blockers, ACE-I, warfarin

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

AF-CHF Trial



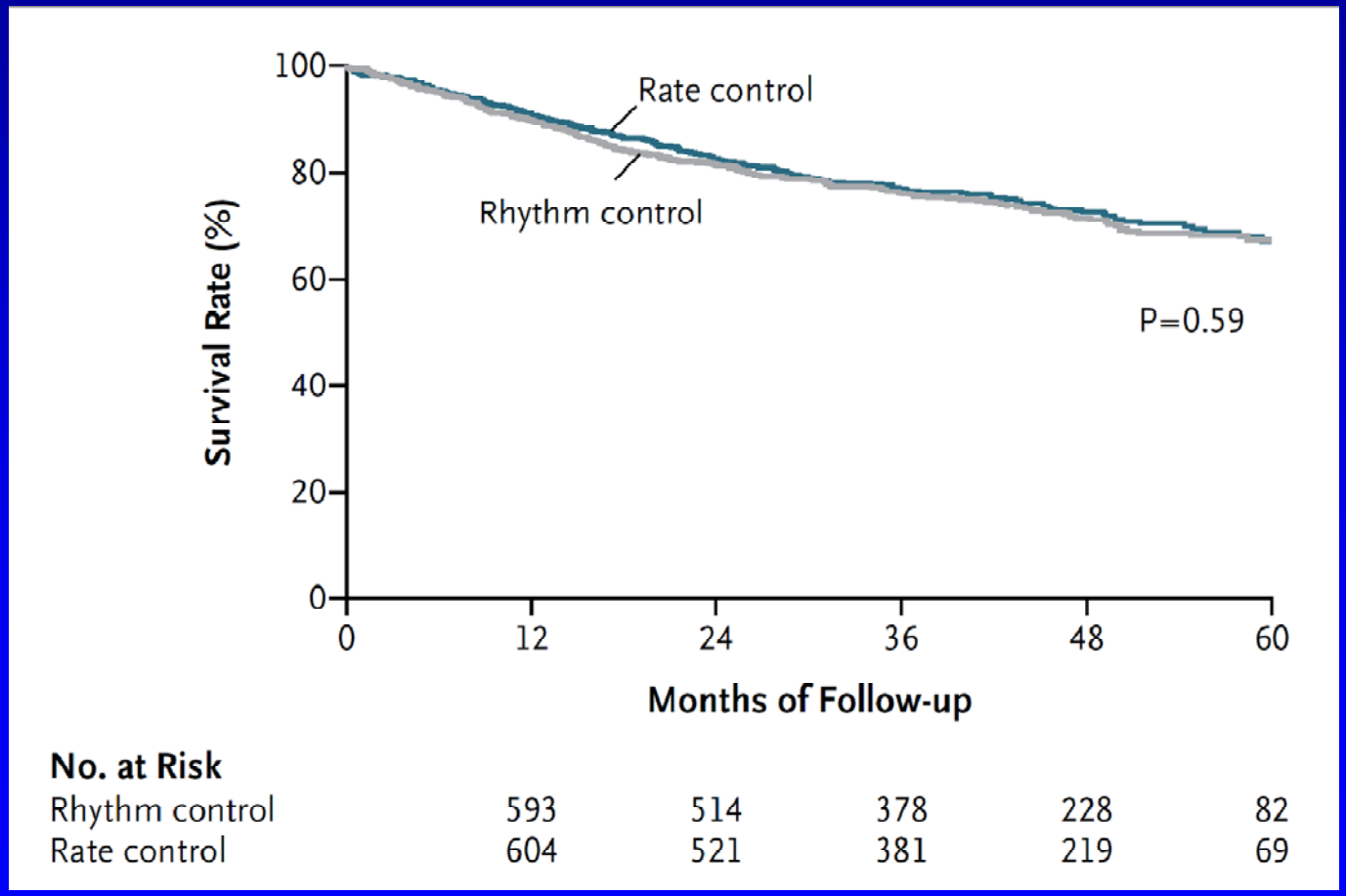
No. at Risk

Rhythm control	593	514	378	228	82
Rate control	604	521	381	219	69

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

AF-CHF Trial

No difference in CV Death



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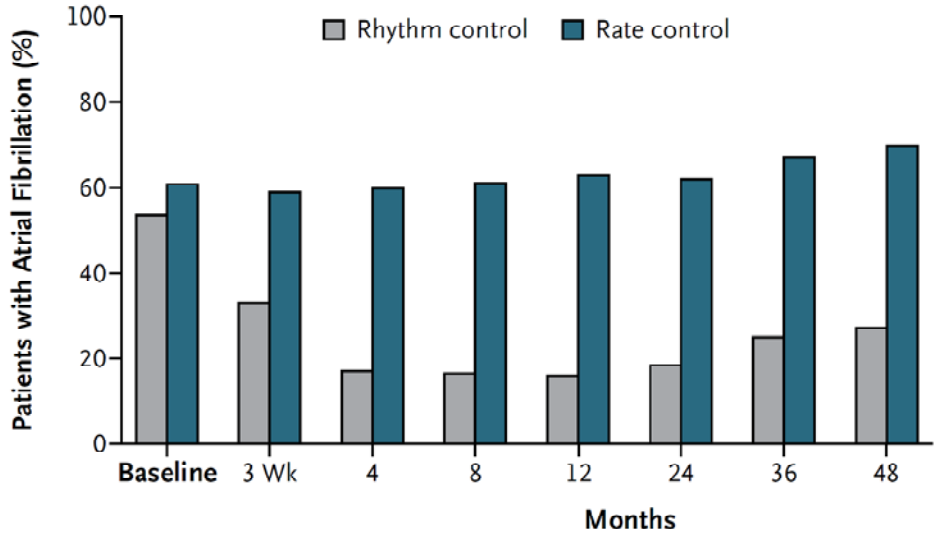
AF-CHF Trial - Results

Drug	Rhythm-Control Group (N = 682)	Rate-Control Group (N = 694)	P Value
	percent		
Amiodarone	82	7	<0.001
Sotalol	2	<1	0.02
Dofetilide	<1	<1	0.62
Beta-blocker	80	88	<0.001
Digoxin	51	75	<0.001
Verapamil or diltiazem	2	3	0.10
ACE inhibitor	81	82	0.41
ARB	16	13	0.09
ACE inhibitor or ARB	94	94	0.57
Diuretic	80	82	0.37
Aldosterone antagonist	47	49	0.51
Oral anticoagulant	88	92	0.03
Aspirin	34	31	0.31
Lipid-lowering drug	44	46	0.61



Participants in rhythm control less likely to have AF than those in rate control

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

Rhythm Control - AF-CHF Trial

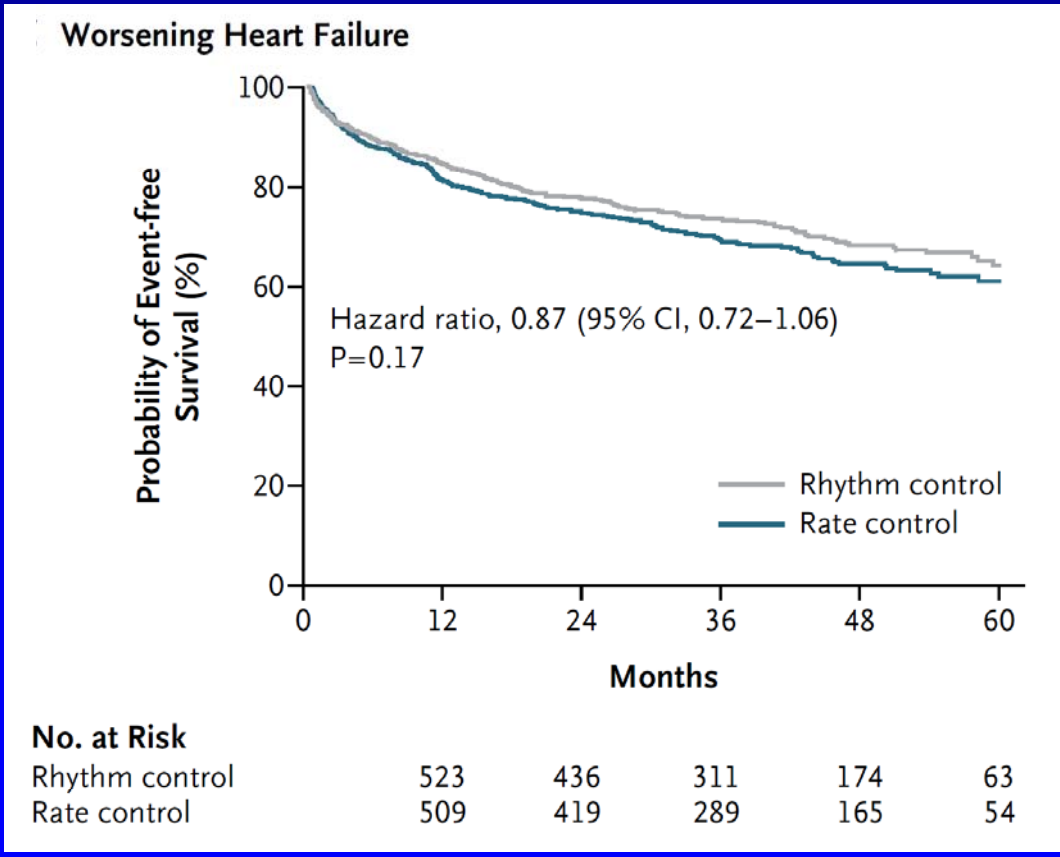
Secondary endpoints

- More hospitalizations (64% vs 59%, p = 0.06), mainly during the first year (46% vs 39%, p = 0.001)
  - More AF hospital stays (14% vs 9%, p = 0.001)
  - More bradycardia hospital stays (6% vs 3%, p = 0.02)
- More cardioversions (59% vs 9%, p < 0.001)
- Less noncardiovascular death - rate control (8% vs 5%, p = 0.06, near significant)

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

AF-CHF Trial

- 21% crossed over rhythm to rate control arm (inability to maintain sinus)
- 10% crossed over rate to rhythm control arm (worsening CHF)



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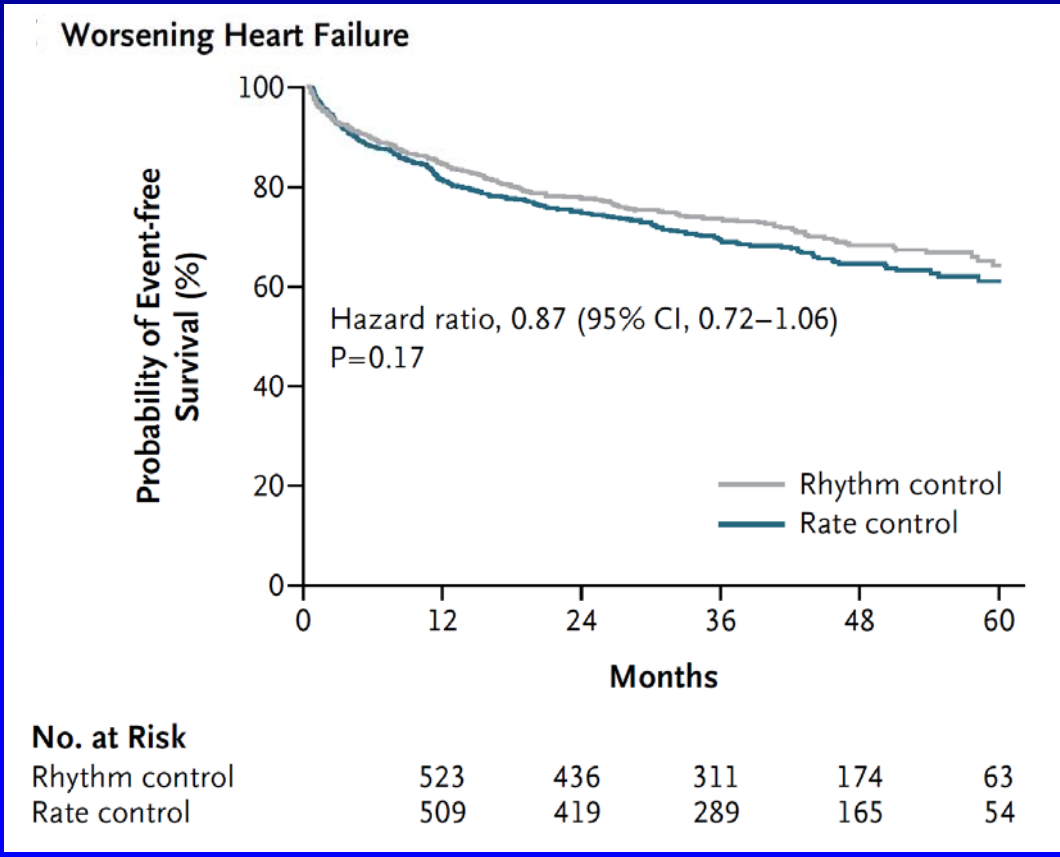

No difference in CHF - intention-to-treat analysis

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

AF-CHF Trial

	Cardiovascular Death		Total death	
Covariate	Hazard Ratio (95%CI)	p	Hazard Ratio (95%CI)	p
AF vs Sinus	1.22 (0.80–1.87)	0.348	1.11 (0.78–1.58)	0.568
NYHA (3–4 vs 1–2)	1.78 (1.16–2.73)	0.008	1.88 (1.31–2.69)	<0.001
Coronary Disease	2.00 (1.29–3.08)	0.002	2.23 (1.54–3.23)	<0.001
Prior stroke	2.47 (1.41–4.34)	0.002	2.23 (1.38–3.62)	0.001
Mitral Regurgitation	2.02 (1.33–3.08)	0.001	1.65 (1.15–2.35)	0.006
Warfarin Use	0.38 (0.23–0.65)	0.001	0.48 (0.30–0.77)	0.003

- AF did not predict mortality in a time-dependent covariate in a multivariate model

Talajic M. Circulation 2008;118:S827

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AF-CHF Trial

- Few were NYHA class III or IV at enrollment
- None had decompensated CHF
- LVEF was depressed in all patients
- Unclear number receiving pacers, CRTs, ICDs

Best treatment for AF in severe or acutely decompensated CHF or CHF with preserved LVEF remains undefined

AF-CHF Trial

- Heart rate definition similar to AFFIRM
  - 82-88% of participants in rate control achieved the goal during 3-year follow-up[1]
  - Only β-blockers and digoxin used
- Less strict heart rate definition may be as effective in AF patients (RACE vs AFFIRM)[2]

1. Roy D. N Engl J Med 2008;358:2667-77
2. Rienstra M. Eur Heart J 2007;28:741-51

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Best target heart rate of AF in CHF uncertain

1. Roy D. N Engl J Med 2008;358:2667-77
2. Rienstra M. Eur Heart J 2007;28:741-51

AFFIRM and AF-CHF

How Do They Compare?

- Similarities
  - Large, randomized, multi-center trial of AF patients
  - Patient age
  - Rate vs rhythm control
  - Rate/rhythm goals
  - Patients reaching target
  - Standard drugs used
  - Endpoints
- Differences
  - AF-CHF - CHF only by design
  - Drugs more limited in AF-CHF

AF-CHF - Implications

- No mortality difference (or worsening CHF) between rhythm or rate control for patients with AF and CHF
- More hospitalizations in rhythm control arm

Rate control is a reasonable strategy for AF in CHF

Problems with AF-CHF and AFFIRM

- Wrong endpoint – not the reason AF is treated
- AF may not cause death
- Highly symptomatic patients excluded in both
- Studies do not prove AF is as good as sinus
- Sinus may be better but risk to achieve it may not be worth it
- Cannot apply results to an individual patient

Is Sinus Rhythm the Goal?

Time-Dependant Covariates Associated with Survival

Covariate	*P*-Value	Hazard Ratio	99% CI
Sinus rhythm	<0.0001	0.53	0.39-0.72
Digoxin	0.0007	1.42	1.09-1.86
Antiarrhythmic	0.0005	1.49	1.11-2.01

HR <1.00: decreased risk of death.
HR >1.00: increased risk of death.

In AFFIRM, those achieving sinus may be healthier

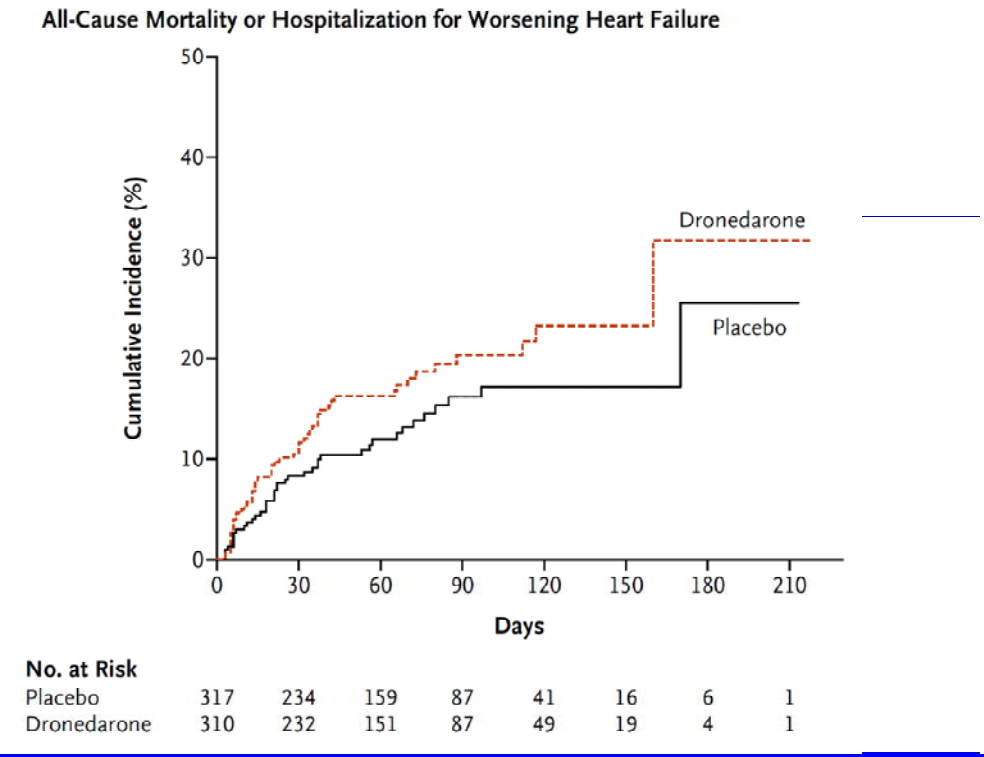
AFFIRM Investigators. Circulation. 2004;109:1509-1513

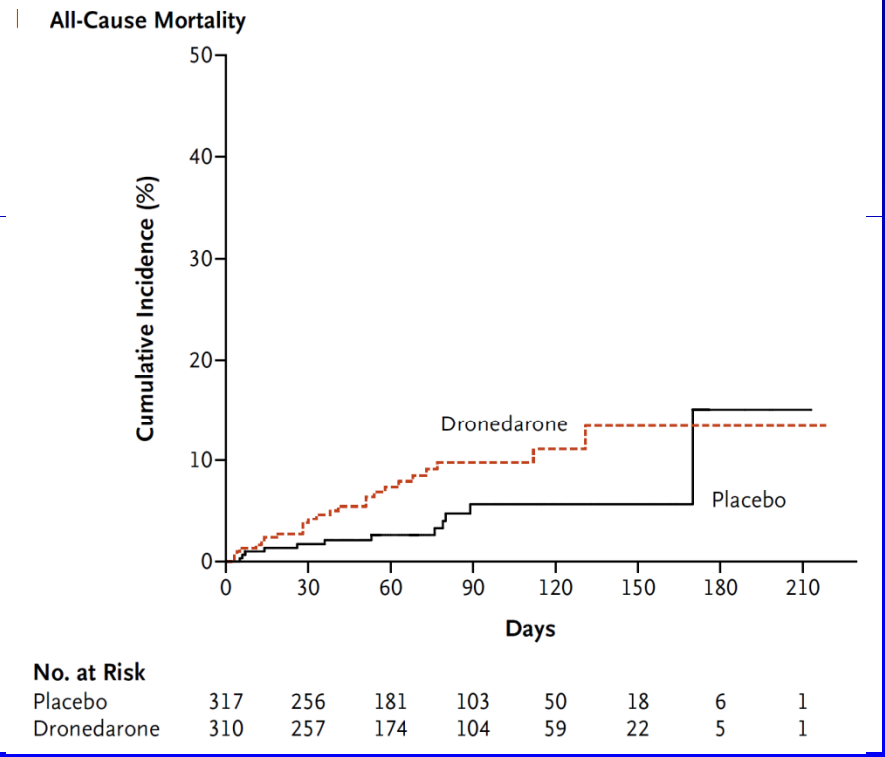
New Antiarrhythmic Drugs

Outcomes May be Drug Dependent

- Dronedarone (de-iodinated amiodarone)
- Azimilide (I_{Kr} and I_{Ks})
- Tedisamil (Pan-K^+ channel blockade)
- H 345/52 (I_{Kr} and I_{Ca})
- SB 207266 (5-HT_4 receptor blocker)
- SB 237376 (K^+ and Ca^{2+} channel blocker)
- RSD1235 (atrial selective, frequency-dependent block of Na^+ and K^+ currents)

ANDROMEDA Trial





- Inclusion: New/worsening CHF (NYHA class III/IV, LVEF ≤0.35)
- AF not an inclusion criteria

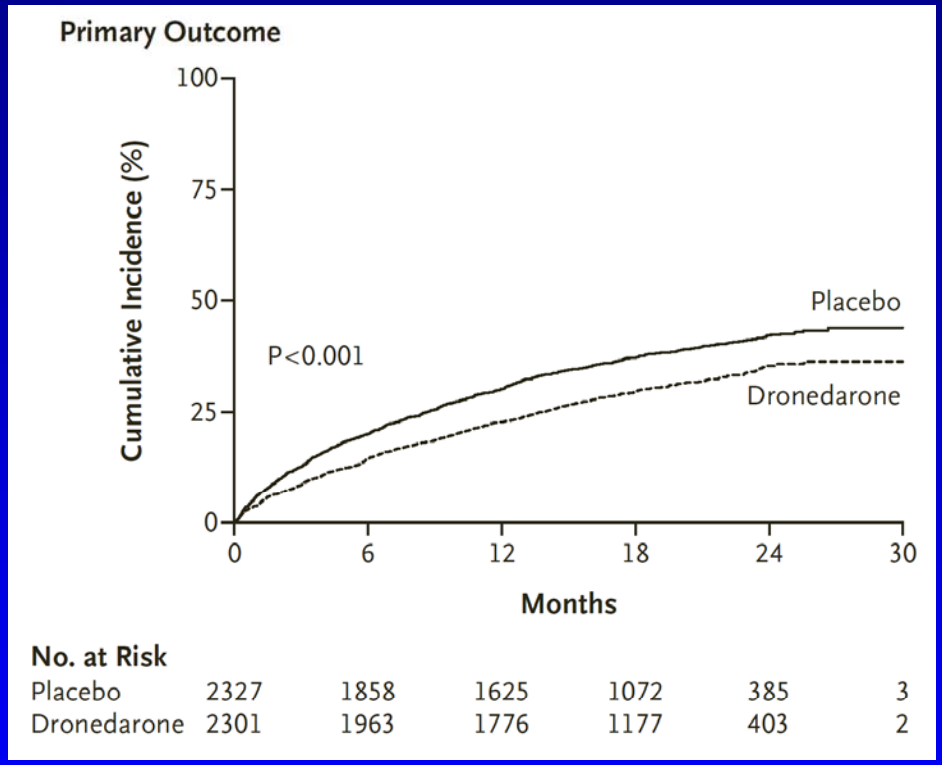
Kober L. N Engl J Med 2008;358:2678-87

ATHENA Trial

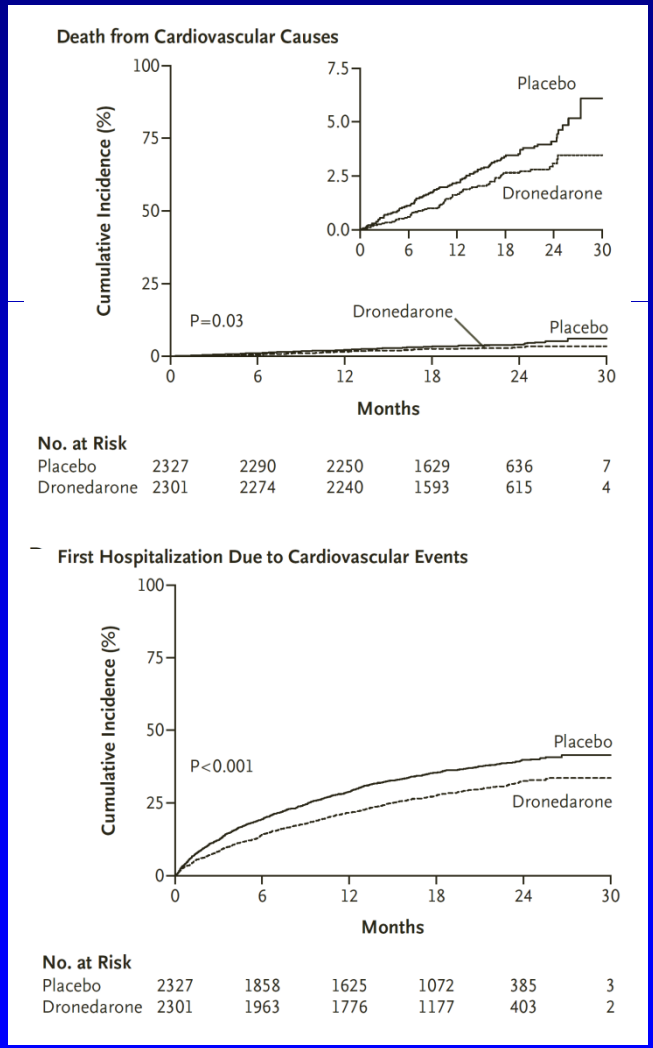
- 4628 patients with AF and risk factor for death
- Randomized to receive dronedarone or placebo
- Combined endpoint - CV hospitalizations and death
- 21% had history of NYHA class II or III CHF
- 11.9% had LVEF ≤0.45 and 3.9% had LVEF ≤0.35

Hohnloser SH. N Engl J Med 2009;360:668-78

ATHENA Trial



Dronedarone decreased composite endpoint but also CV death and hospitalizations



Hohnloser SH. N Engl J Med 2009;360:668-78

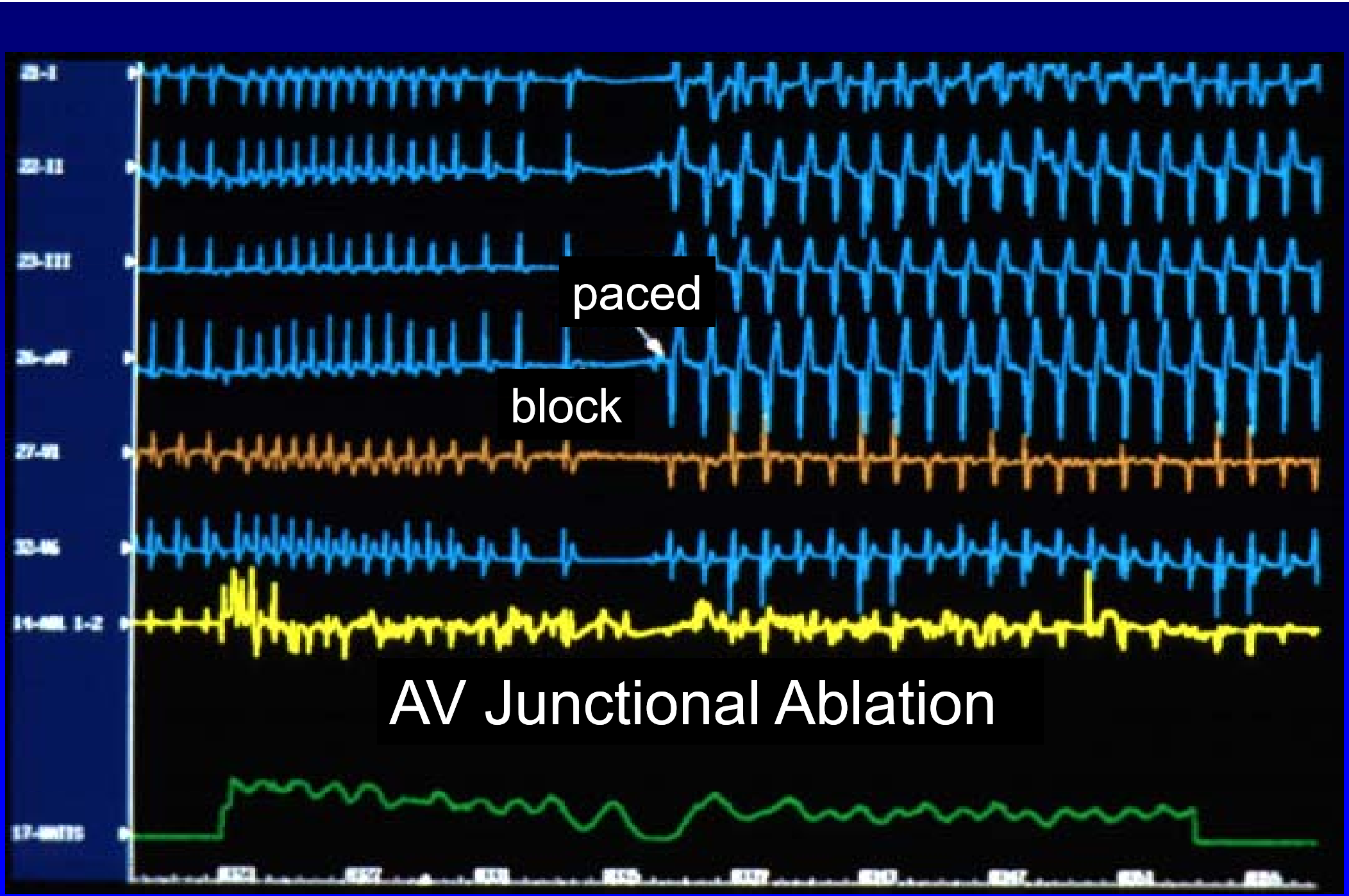
Dronedarone

- Dronedarone can decrease hospitalizations and CV death in patients with AF but without decompensated CHF
- Dronedarone should not be used in acute CHF

Non-Pharmacologic Approaches to AF

Not carefully tested in AF-CHF or AFFIRM

- AV junctional ablation with pacemaker
- AF ablation


paced
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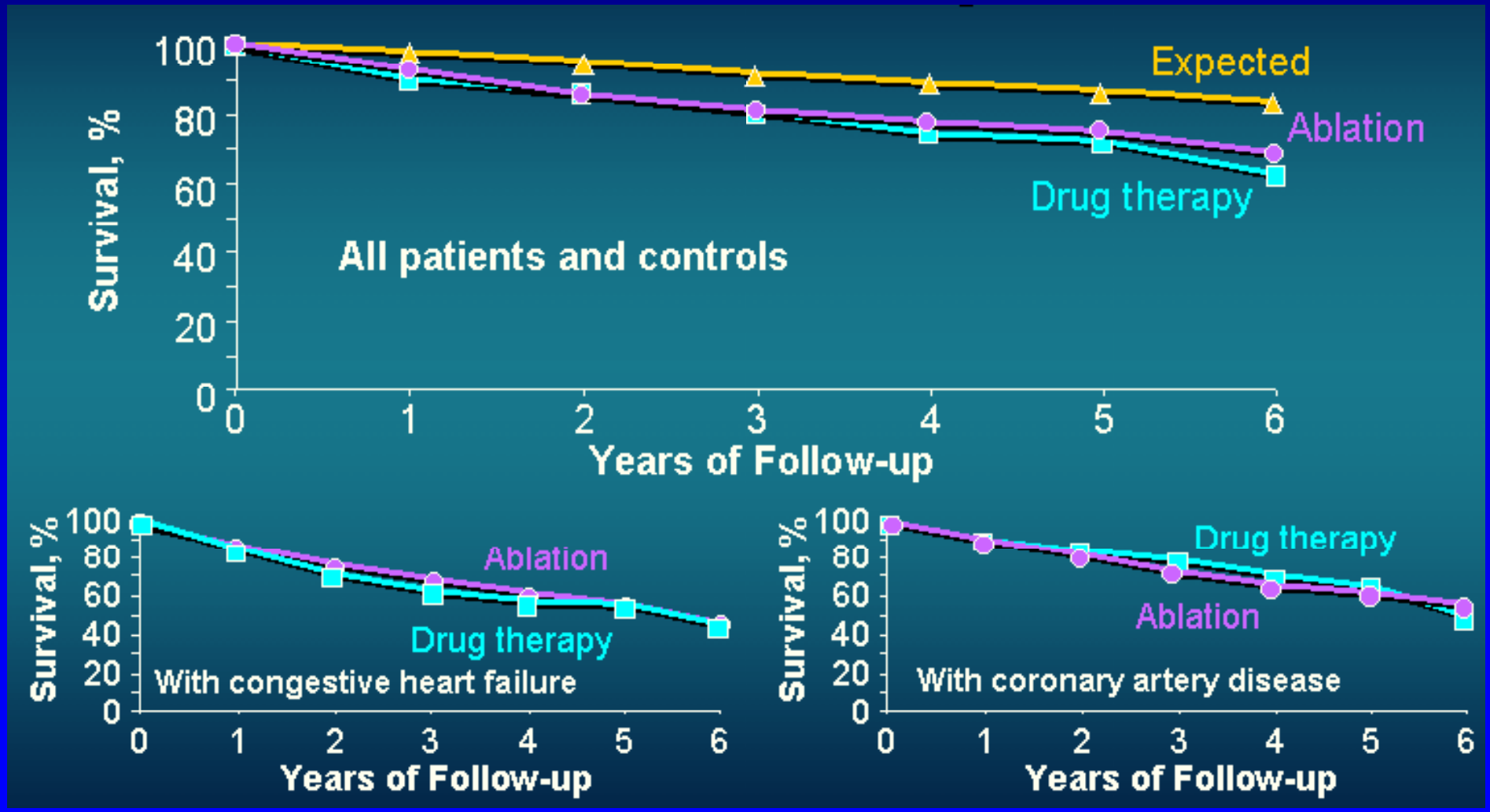
AV Junctional Ablation

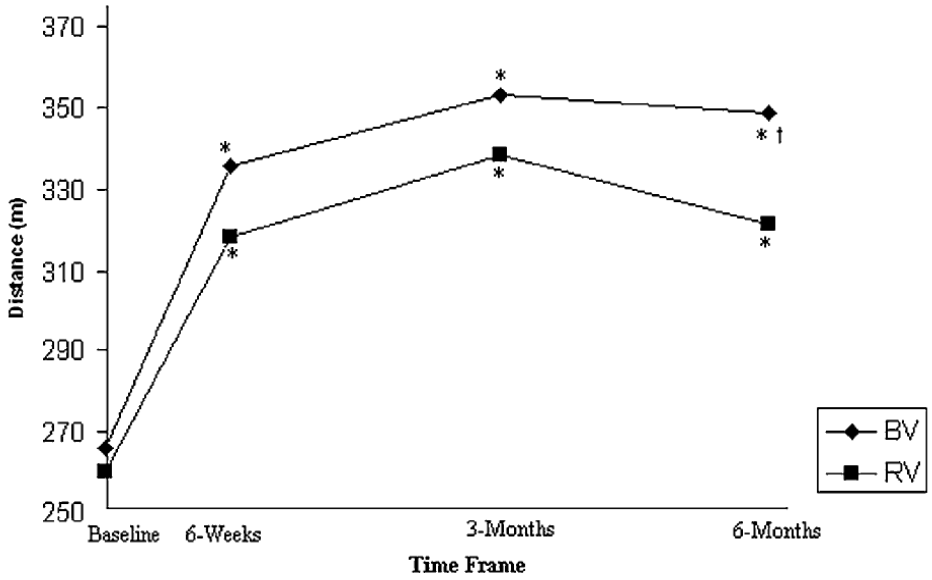
AV Junctional Ablation

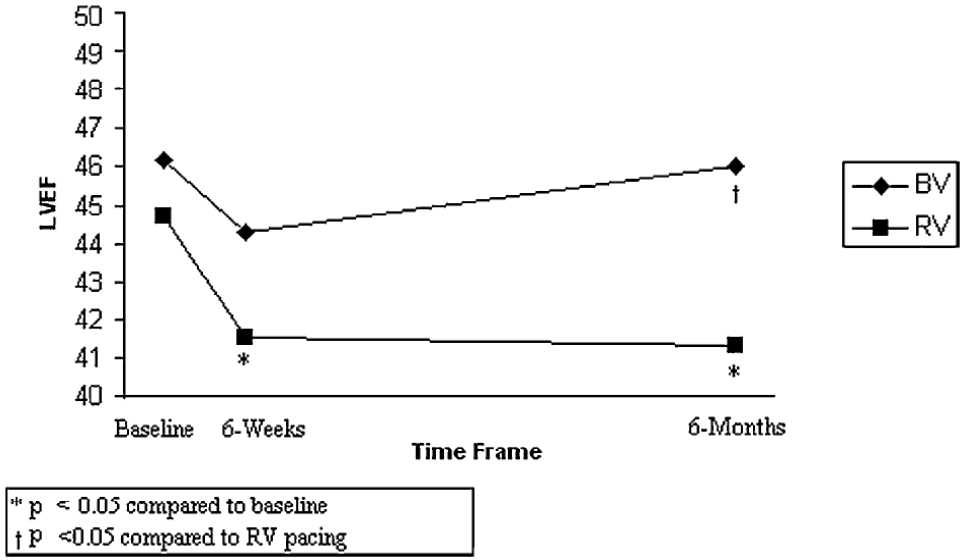


Ozcan C. N Engl J Med 2001;344:1043-1051

AV Junctional Ablation

BiV, VVI?

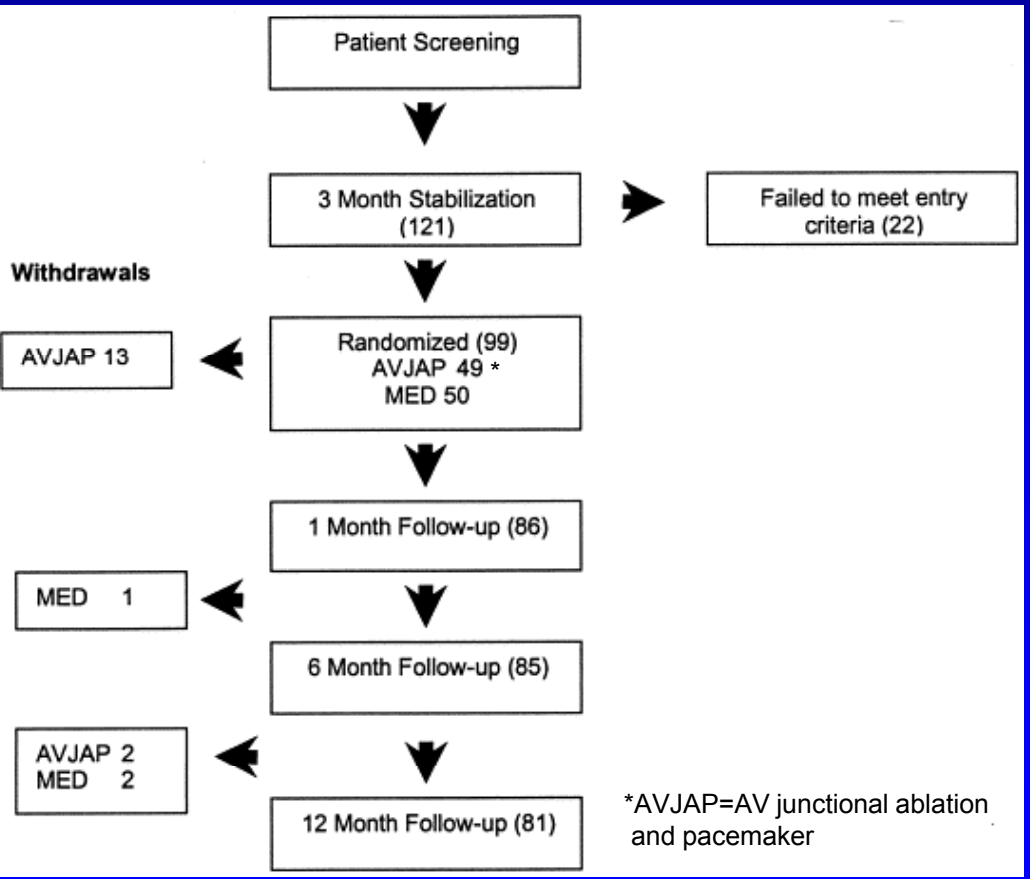




Doshi RN. J Cardiovasc Electrophysiol 2005;16:1160-1165

AIRCRAFT Trial

Is Ablate and Pace the Way to Go?



Results

- LVEF, exercise time same both groups.
- Peak rate lower in AVJAP group with exercise and daily activities ($p<0.05$).
- AVJAP group less symptoms ($p = 0.004$)
- QOL using the "ladder of life" 6% better in AVJAP group ($p = 0.011$).

Conclusions

Ablate/pace in symptomatic permanent AF patients did not worsen cardiac function. QOL improved.

Weerasooriya R. J Am Coll Cardiol 2003;41:1703-6

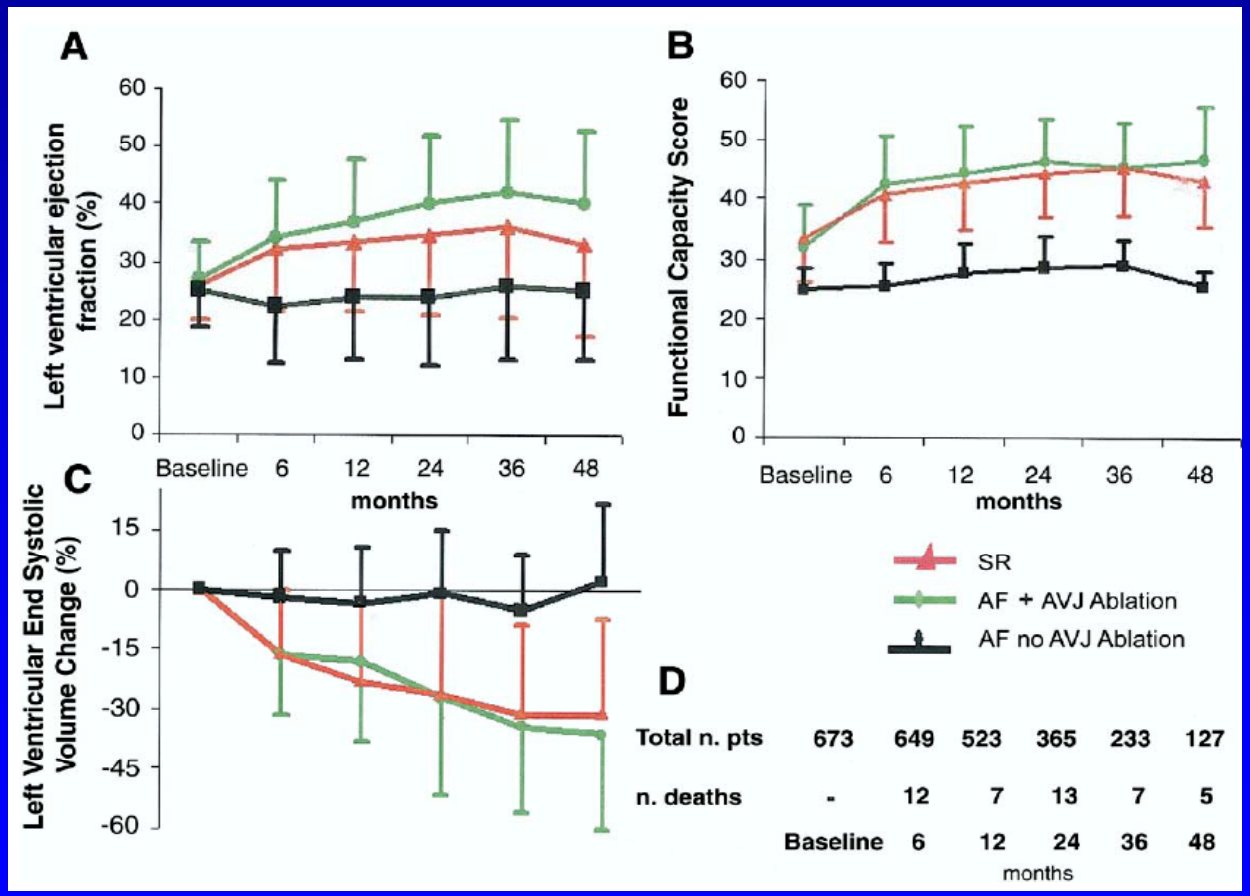
AVERT - AF

- Prospective, multicenter, randomized, double blind trial of 180 patients with AF, class II/III CHF and ejection fraction ≤ 0.35
- Hypothesis: AVJ ablation with CRT ICD improves exercise capacity and functional status vs. pharmacologic rate control (and ICD) in CHF patients with chronic AF.

Hamdan M. PACE 2006; 29:1081–1088

CRT Works in Atrial Fibrillation

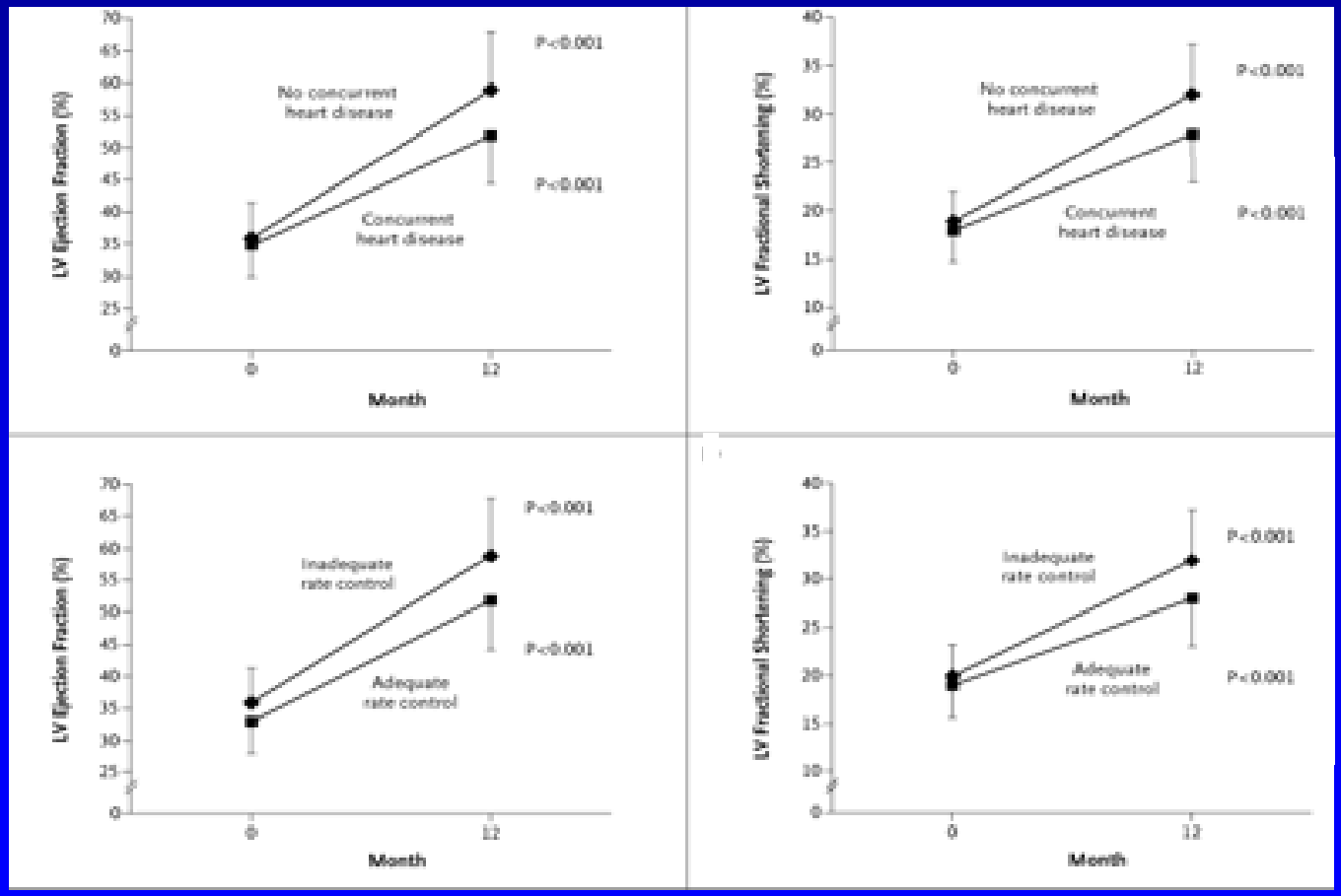
AV Junctional Ablation Needed in 49 - 70%



Gasparini M. J Am Coll Cardiol 2006;48:734-743

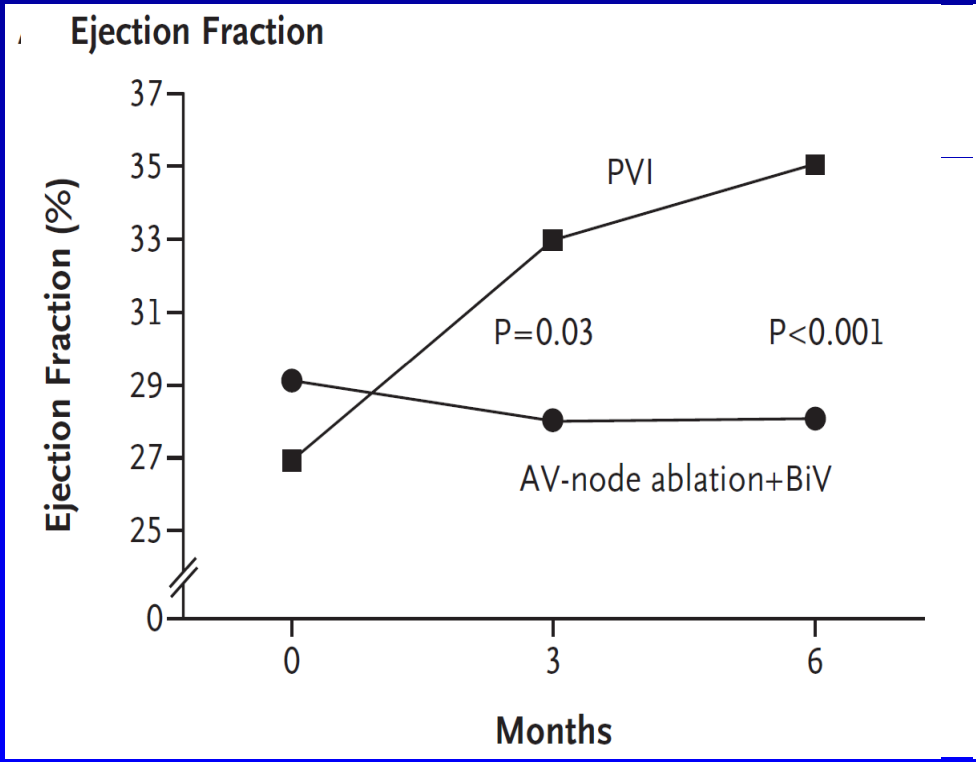
AF Ablation in CHF

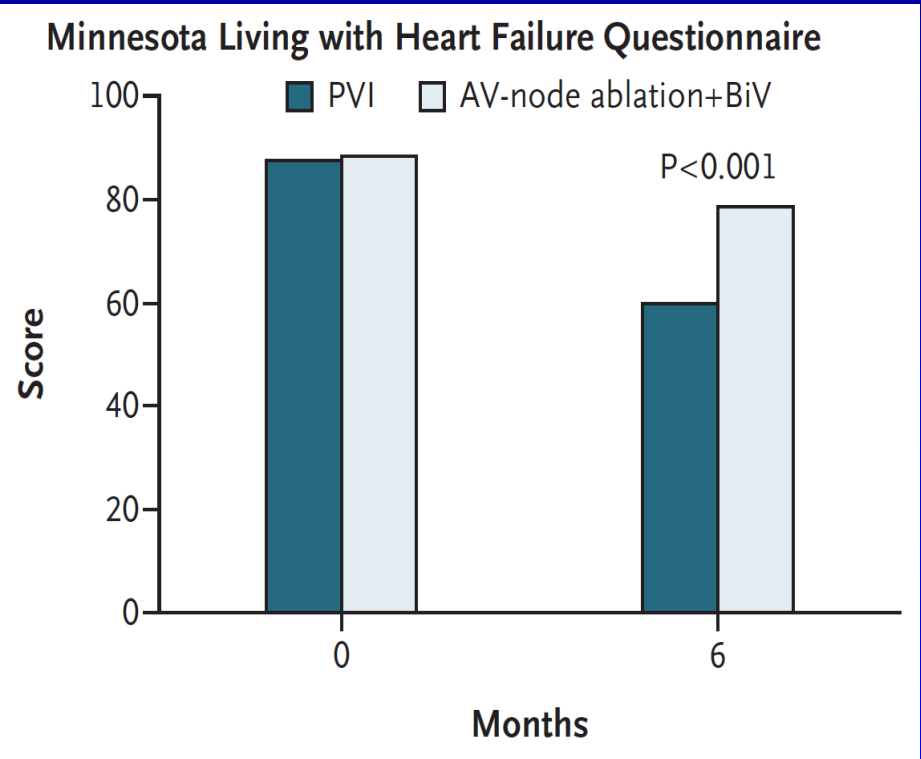
Improved Markers of Ventricular Function



Hsu LF. N Engl J Med 2004;351:2373

Pulmonary Vein Isolation vs AVN Ablation with Bi-Ventricular Pacing





Khan M. N Engl J Med 2008;359:1778-1785

Typical Day at the Office

- 75 yo female, non-ischemic cardiomyopathy
  - NYHA FC III heart failure; EF 0.30; s/p CRT-D
- Recent ICD shocks
- BP: 144/94, P 120, irregular
  - Heart: S1, S2, S3; Lungs: bibasilar rales
- EKG – atrial fibrillation, LBBB (unpaced)

What have we learned?

AF and CHF in 2009

Bottom Line for the Average Patient

- Rhythm control ± anticoagulation when there are intolerable symptoms or hemodynamics
- Rate control ± anticoagulation - acceptable
- New drugs - being developed
- Ablation - rapid progress with hope for a cure