Atrial Fibrillation and Congestive Heart Failure

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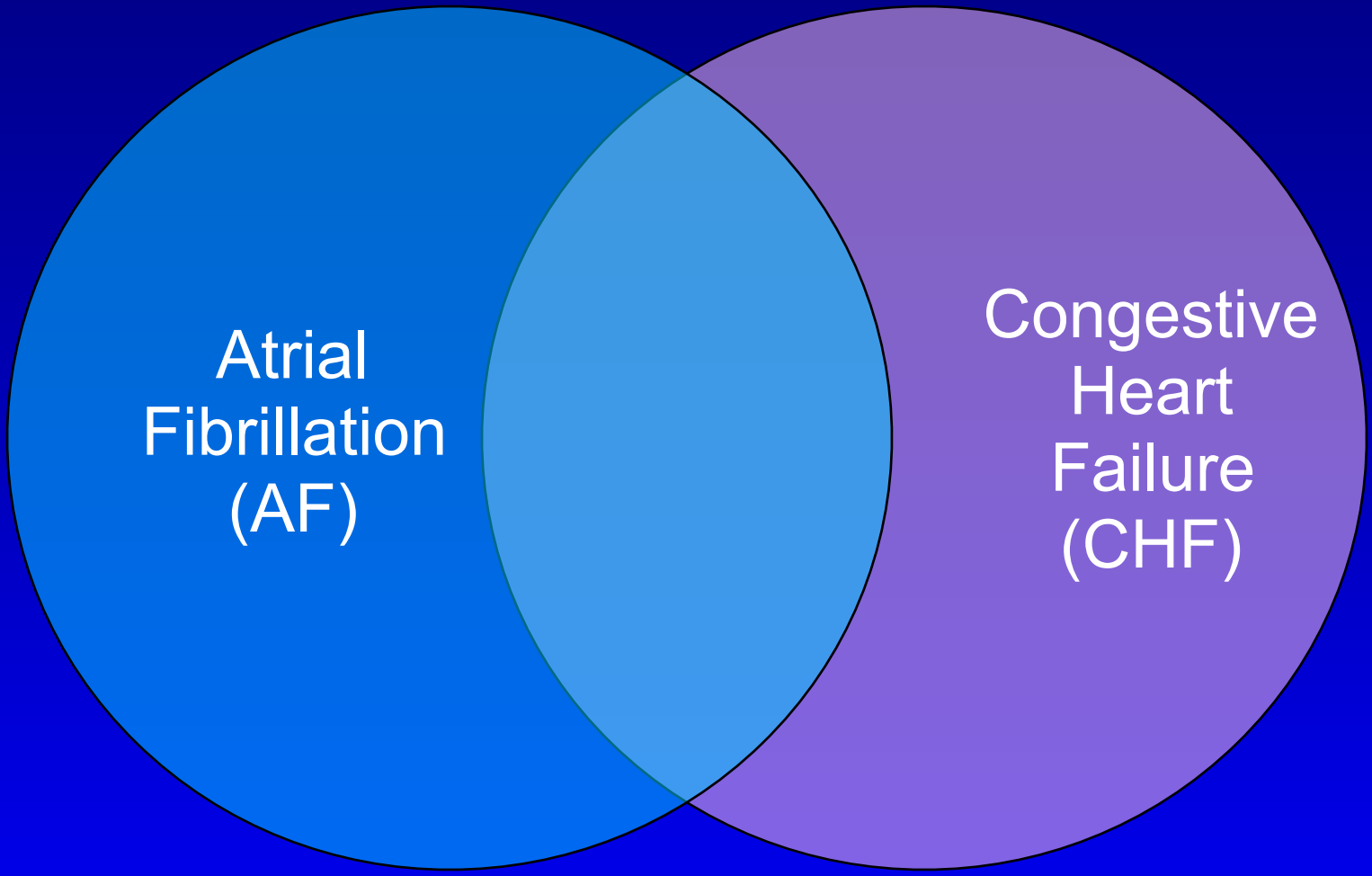
Typical Day at the Office

- 75 year old female, CHF (NYHA FC II), non-ischemic cardiomyopathy (EF = 0.30), s/p DDD ICD, has recent ICD shocks
- BP: 144/94, P 120, irregular
  - heart: S1, S2, S3
- EKG – LBBB, atrial fibrillation

What Do You Do Now?

Lots of questions

- Admit? Then what?
- Rate control. How?
- Anticoagulate. How?
- Cardiovert. How? When? Why?
- Start an antiarrhythmic. How? Where?
- Ablate. What?
- Upgrade ICD?



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

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

CHF: Prevalence of AF

Systolic Dysfunction

- AF in 6-10% mild and >40% advanced CHF patients
- Left ventricular dysfunction increases risk of AF 4.5x (men) 5.9x (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

AF & CHF – Hospitalized Patients

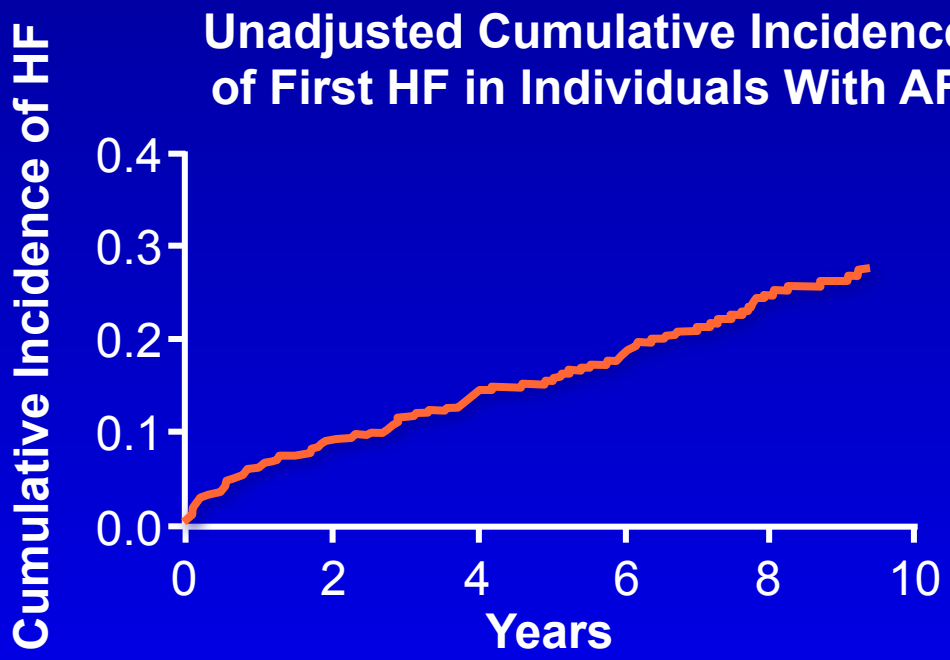
National Hospital Discharge Summary

	Age 35 to 64 Years (n=99 440)*		Age ≥65 Years (n=277 047)*	
Diagnosis (ICD-9-CM)	n	%	n	%
Essential hypertension (401)	36 357	36.6	130 216	47.0
Ischemic heart disease (410 to 414)	18 055	18.2	85 209	30.8
Congestive heart failure (428)	13 057	13.1	59 412	21.4
Other cardiac dysrhythmias (427)	16 161	16.3	47 754	17.2
Diabetes mellitus (250)	16 350	16.4	40 212	14.5
Chronic airway obstruction (496)	6473	6.5	35 983	13.0
Valve disorders (424)	6669	6.7	34 205	12.3
Postsurgical statest†	9600	9.7	34 202	12.3
Disorders of lipoid metabolism (272)	10 082	10.1	30 916	11.2

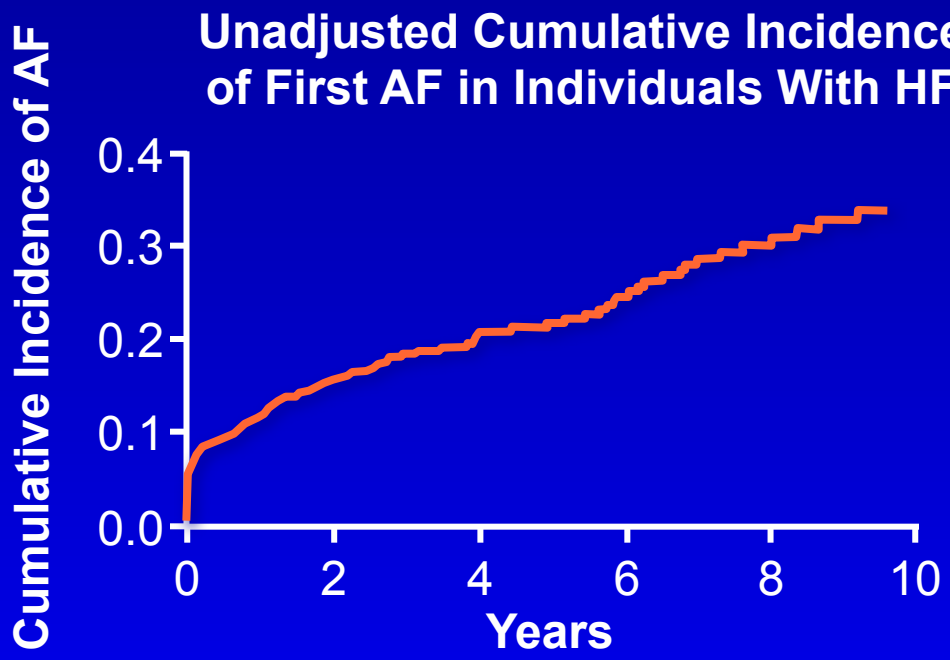
Wattigney WA. Circulation 2003;108;711-716

Relationship of AF and CHF

The Framingham Study



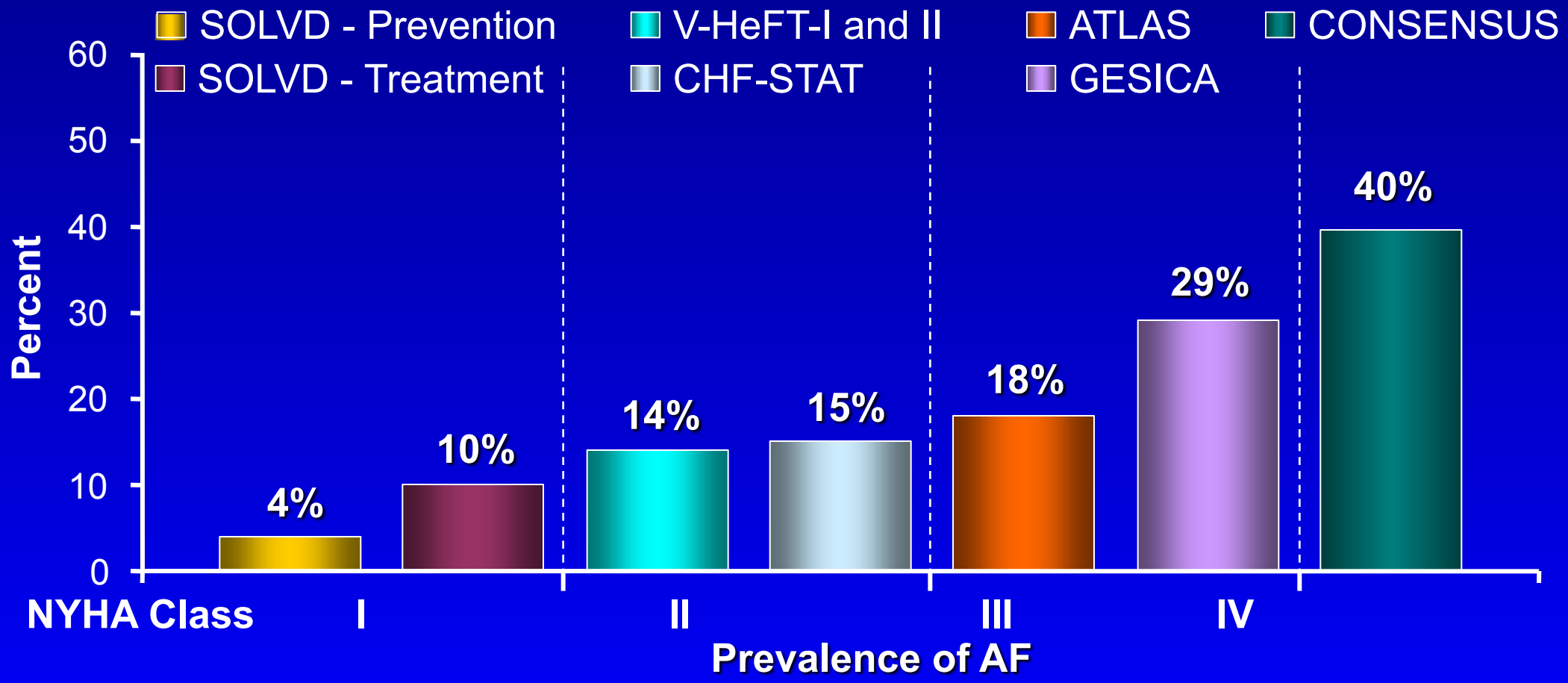
921 with AF
26% prior or concurrent CHF
16% developed CHF



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

Wang TJ. Circulation 2003;107:2920-5

Prevalence of AF in Patients With HF



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

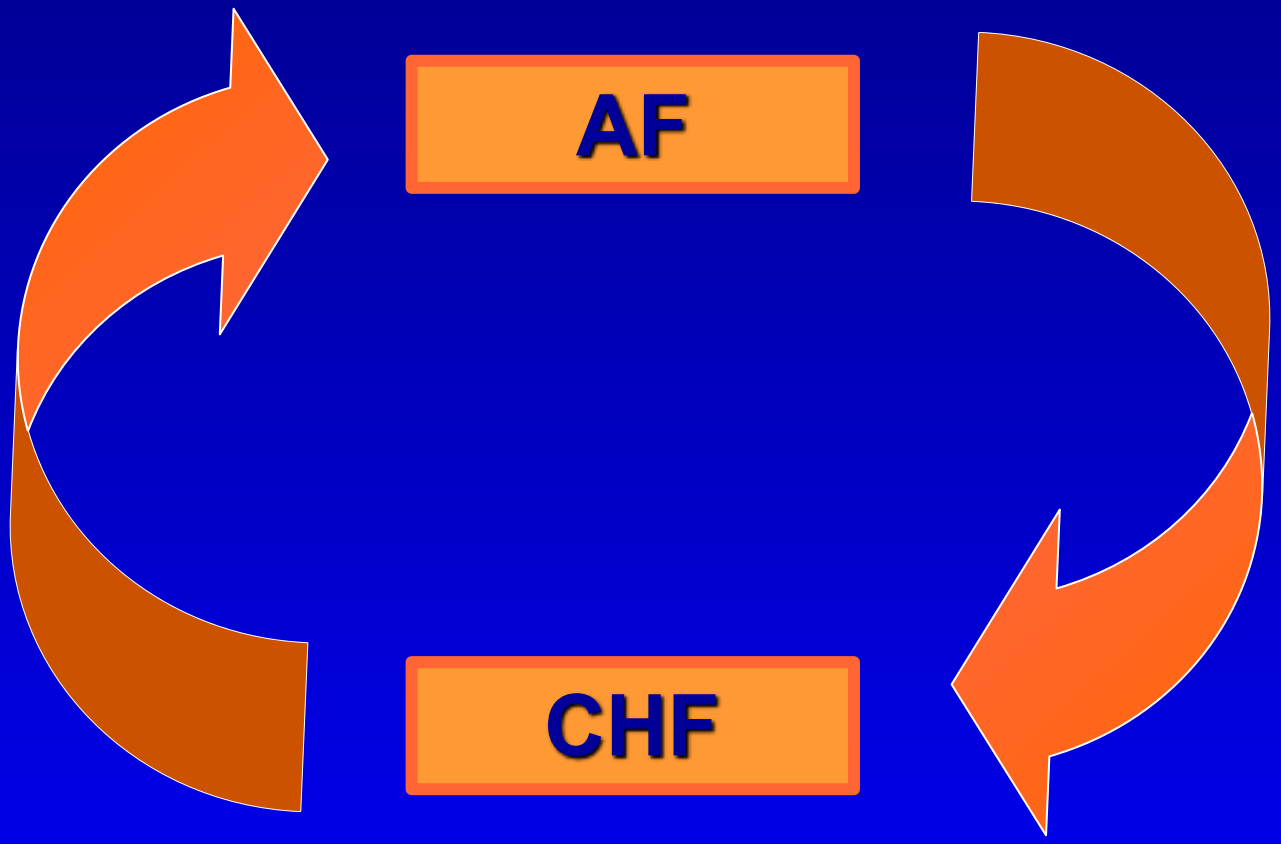
CHF: Prevalence of AF

Diastolic Dysfunction

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

Tsang TS. J Am Coll Cardiol 2002;40:163
Chen HH. J Card Fail 2002;8:279

Mechanisms



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

Relationship: AF and CHF

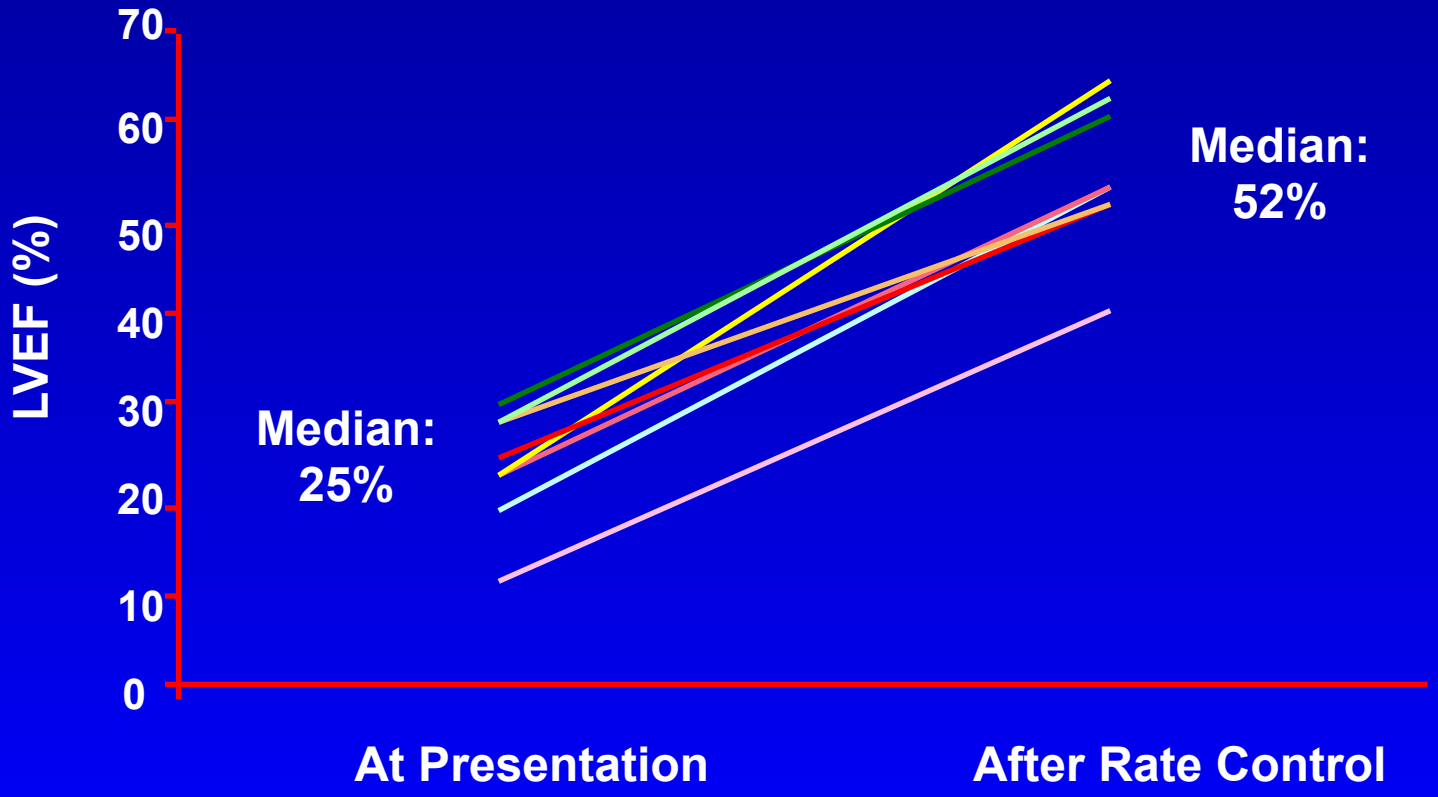
- AF -> CHF
  - Loss of atrial contraction
  - Irregular rate
  - Inappropriate, usually, rapid, rate
- CHF -> AF
  - Increased atrial pressure, stretch, volume
  - Neurohumoral alteration
  - Inflammation, circulating mediators, fibrosis
  - Ion channel/connexin changes

Mechanisms: Chronic AF -> CHF

Rate Dependant Cardiomyopathy

- Depletion of high energy stores
- Activation of sympathetic nervous system and renin-angiotensin system
- Depletion of ATP
- Myocardial ischemia
- Myocyte and extracellular remodeling
- Defects in Ca^{+2} handling

Rate Control in AF: Benefits



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

Heart Failure and Sudden Death in Patients With Tachycardia-Induced Cardiomyopathy and Recurrent Tachycardia

Pamela Nerheim, MD; Sally Birger-Botkin, RN; Lubna Piracha, DO; Brian Olshansky, MD

Background—Tachycardia-induced cardiomyopathy is a reversible cause of heart failure. We hypothesized that although left ventricular ejection fraction measurements normalize after heart rate or rhythm control in patients with tachycardia-induced cardiomyopathy, recurrent tachycardia may have abrupt and deleterious consequences.

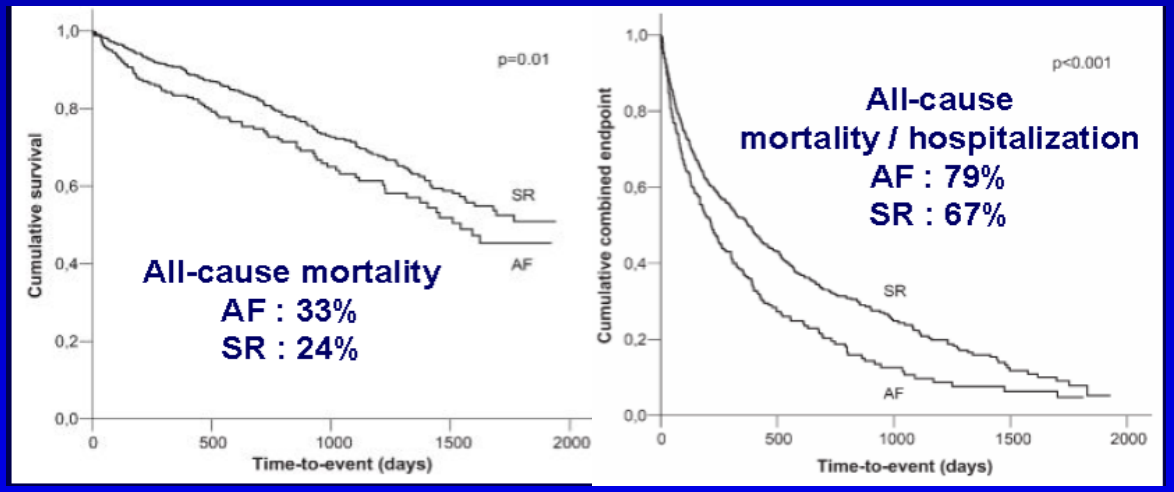
Methods and Results—Patients with tachycardia-induced cardiomyopathy that developed over years were evaluated and treated. Tachycardia episodes and outcomes were assessed. Twenty-four patients were identified. All had NYHA functional class III heart failure or greater on presentation. One third were heart transplant candidates. There were 17 men and 7 women with a mean age of 46±16 years and mean left ventricular ejection fraction of 0.26±0.09 at the index visit. The cause was atrial fibrillation (n=13), atrial flutter (n=4), atrial tachycardia (n=3), idiopathic ventricular tachycardia (n=1), permanent junctional reciprocating tachycardia (n=2), and bigeminal ventricular premature contractions (n=1). Within 6 months of rate control or correction of the rhythm, left ventricular ejection fraction improved or normalized and symptoms abated in all. Five patients had tachycardia recur. In these patients, left ventricular ejection fraction dropped precipitously and heart failure ensued within 6 months, even though the initial impairment took years. Rate control eliminated heart failure and improved or normalized ejection fraction in 6 months. Three of 24 patients died suddenly and unexpectedly.

Conclusions—Tachycardia-induced cardiomyopathy develops slowly and appears reversible by left ventricular ejection fraction improvement, but recurrent tachycardia causes rapid decline in left ventricular function and development of heart failure. Sudden death is possible. (***Circulation***. **2004;110:247-252.**)

Key Words: arrhythmia ■ death, sudden ■ heart failure ■ heart rate ■ tachycardia

Prognostic Influence of AF in CHF

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

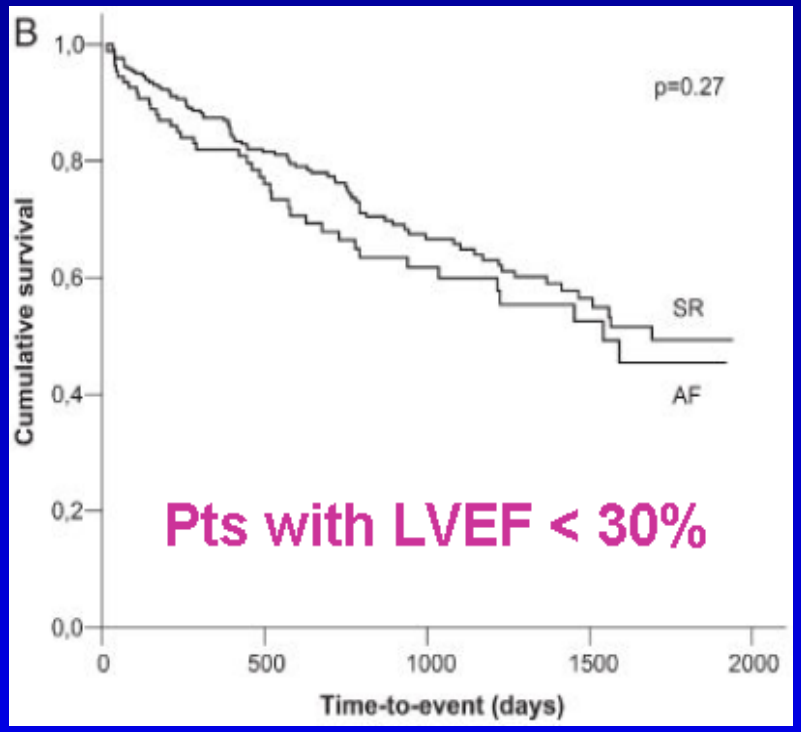


HR for death in AF patients
1.38 (CI: 1.07 – 1.78, p=0.01)

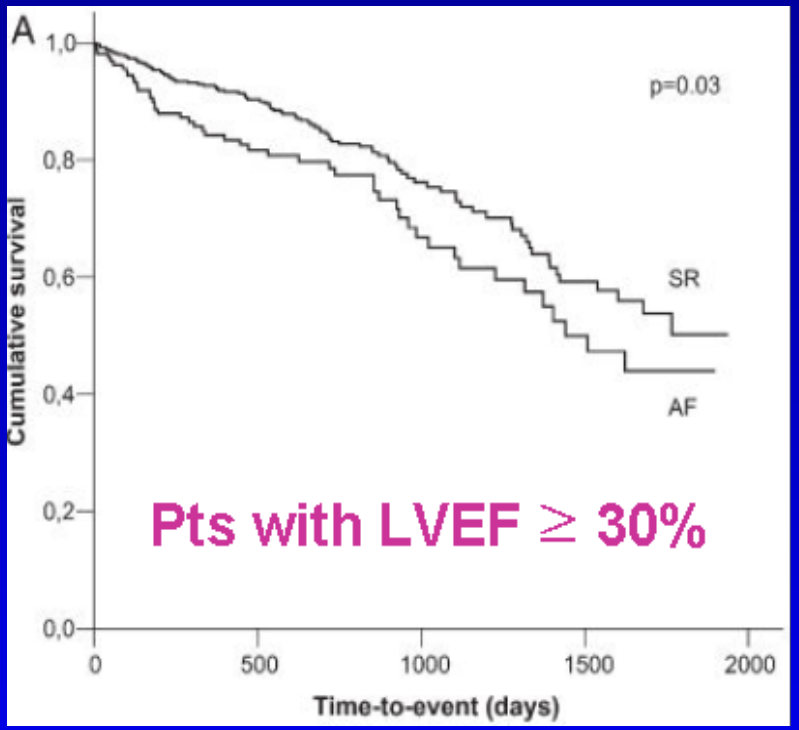
HR = 1.43
(CI: 1.22 – 1.68, p<0.001)

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

Prognostic Influence of AF in CHF



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

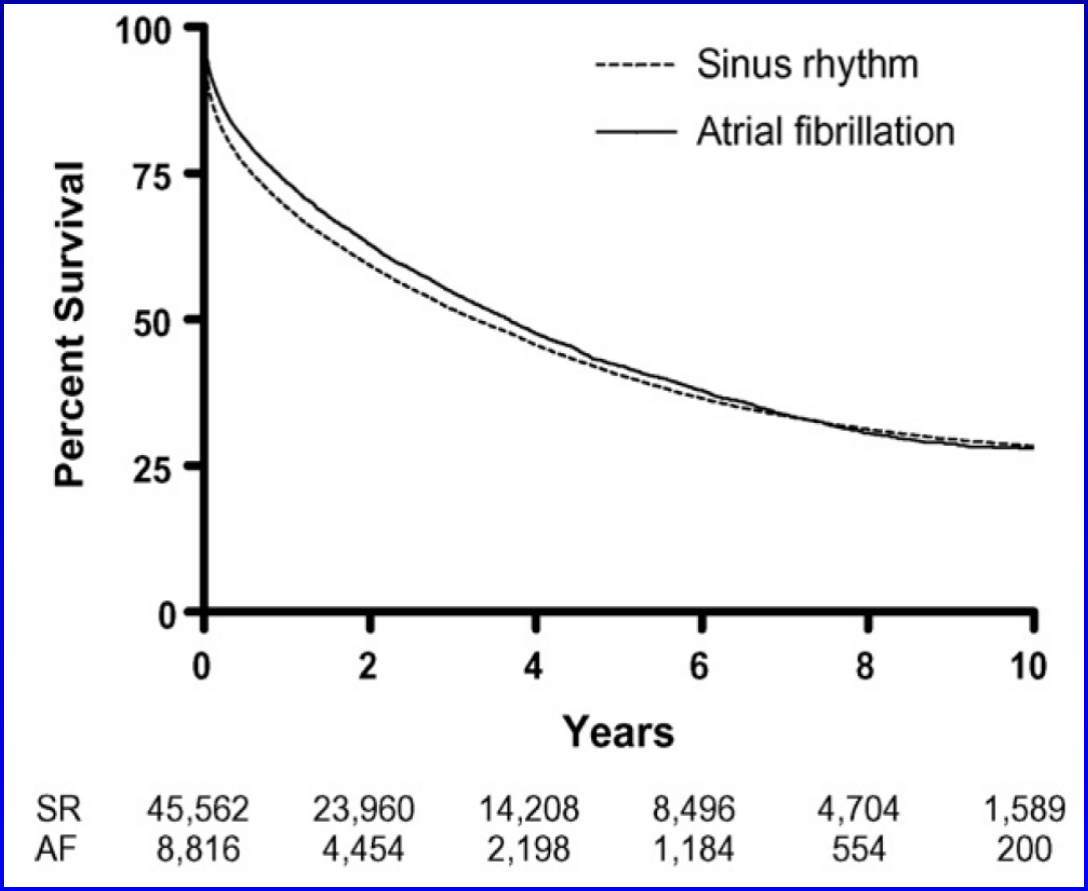


Baseline AF - increased mortality
HR 1.46; CI 1.04-2.07; p=0.03

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

Is AF in CHF Prognostic?

55,106 Admissions - CHF in New Zealand



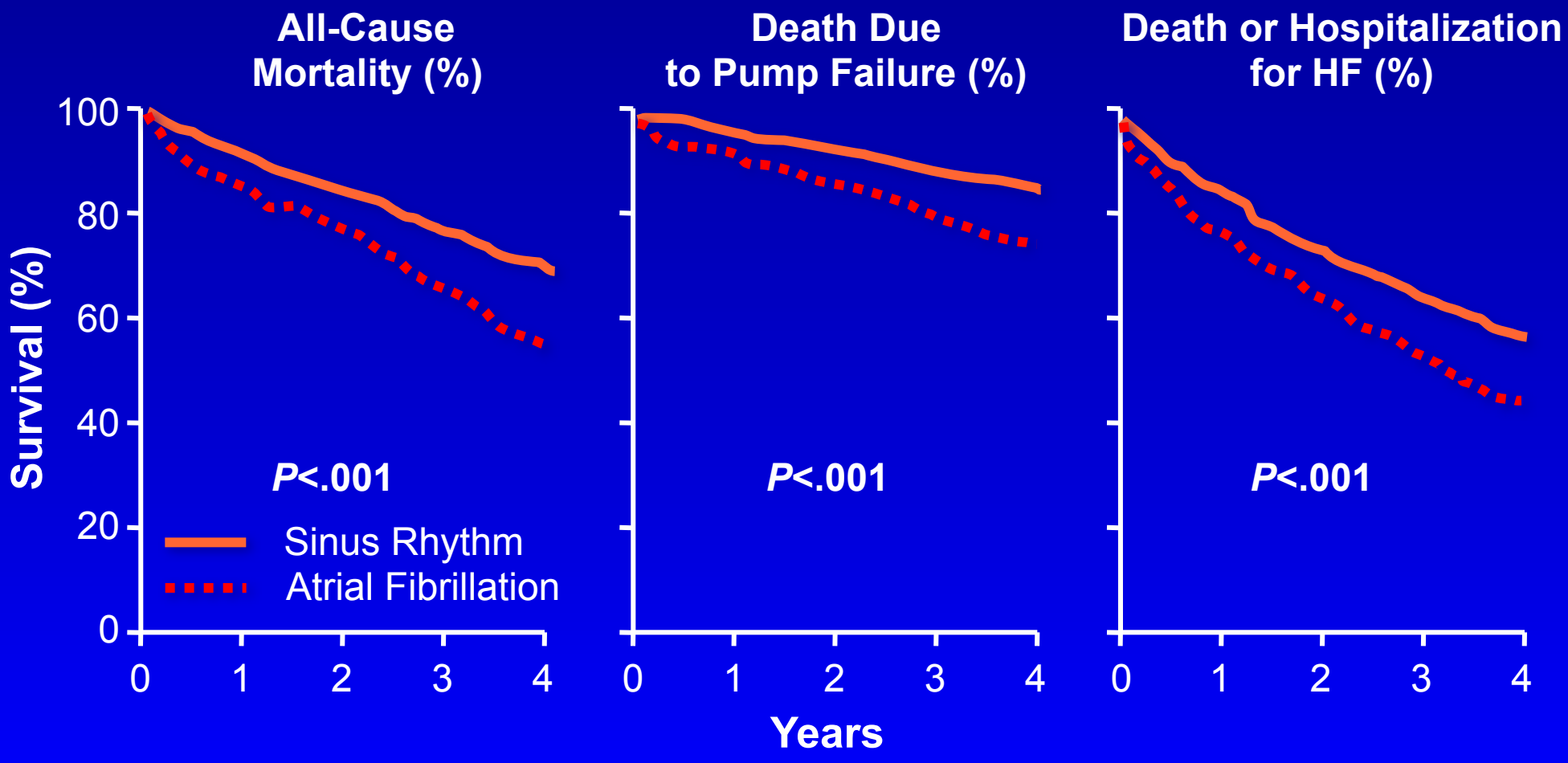
Wasywich CA. Heart Lung Circ 2006;15:353

Prognostic Influence of AF on CHF

- AF associated with higher mortality
  - SOLVD, Framingham, DIAMOND, CHF-STAT, severe CHF[1], elderly[2], CHF post MI[3]
- AF not associated with higher mortality
  - V-HEFT[4], severe CHF[5], heart transplant[6], COMET[7]

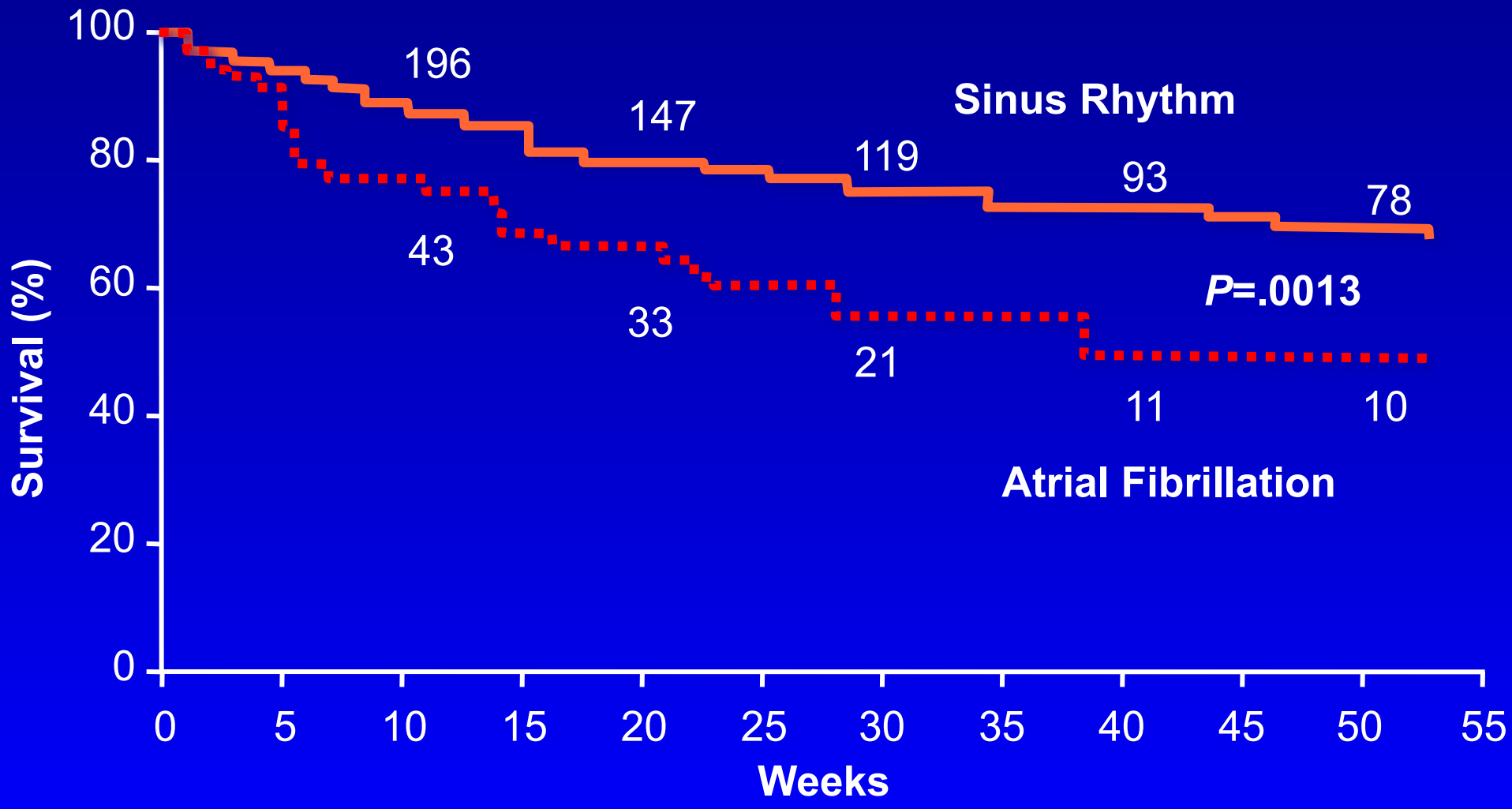
1.Stevenson W J Am Coll Cardiol;1996;28:1458,
2. Ahmed A. Eur J Heart Fail2004;6:421
3. Aronow WS. Am J Cardiol 2001;87:224
4.Carson PE Circulation 1993; 87:VI102
5. Crijns H Eur Heart J 2000;21:1238
6. Mahoney P Am J Cardiol 1999;83: 1544
7. Swedberg K. Eur Heart J 2005;26:1303

AF and Mortality - SOLVD Trial



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

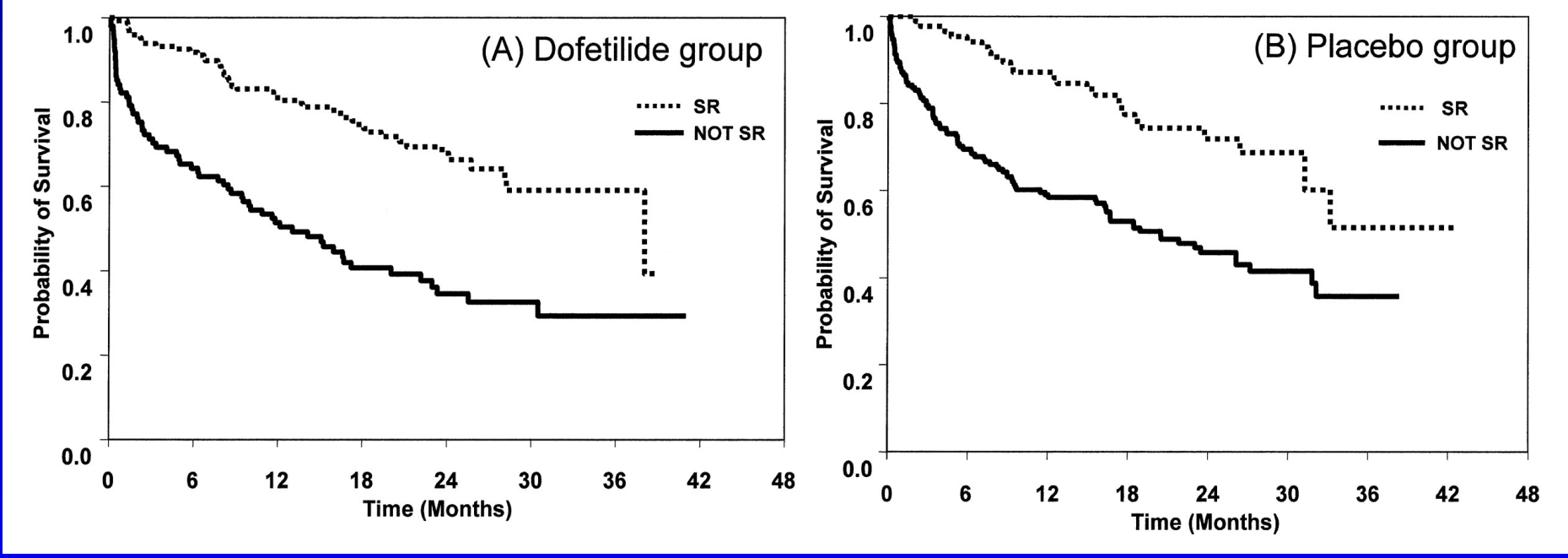
Prognosis of AF in Advanced HF



Middlekauff H. Circulation. 1991;84:40-48

Maintaining Sinus in Patients with Left Ventricular Dysfunction

Dofetilide vs Placebo DIAMOND TRIAL

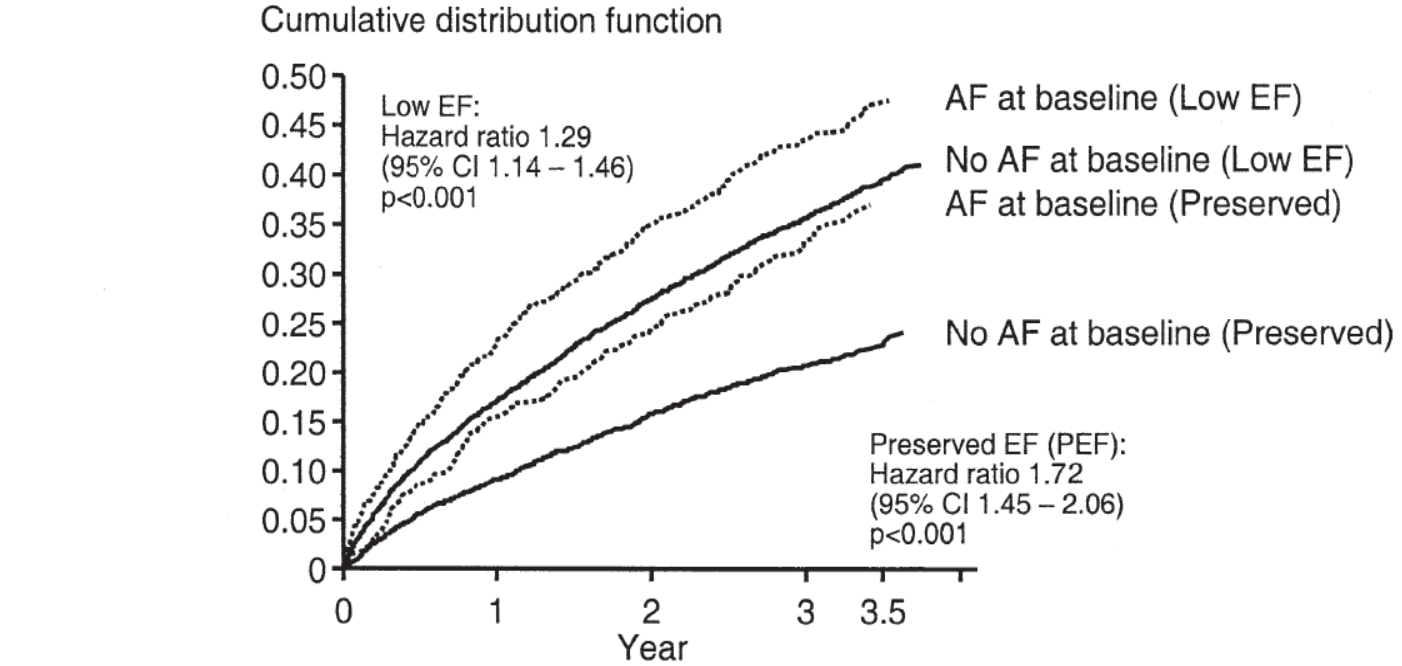


Effect of Sinus on Mortality Multivariate Analysis
RR 0.44 (0.30-0.64); P<0.0001

Pedersen OD. Circulation. 2001;104:292-6

CHARM Trial

AF has Prognostic Significance

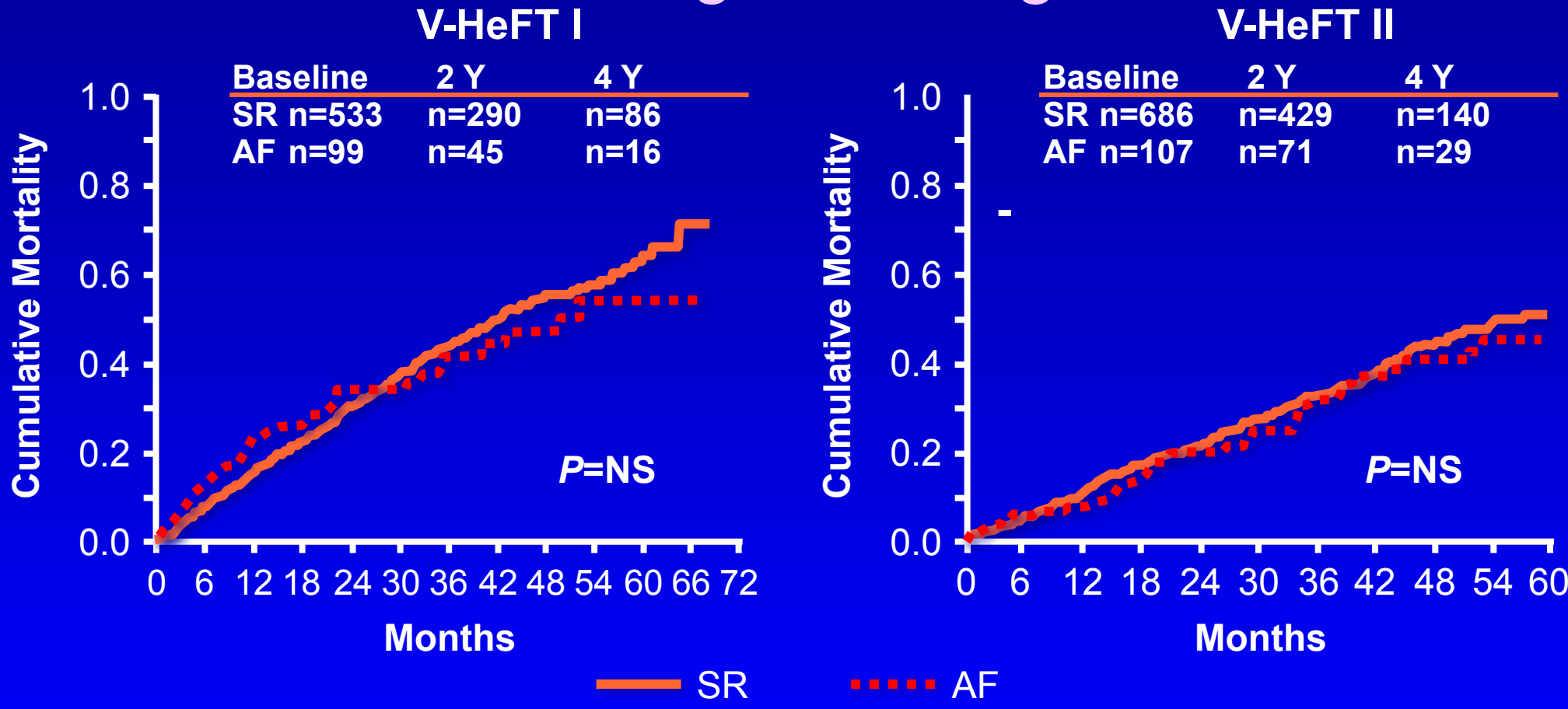


Number at risk				
No AF & Low EF	3906	3207	2755	1963
No AF & PEF	2545	2294	2096	1276
AF & Low EF	670	509	417	289
AF & PEF	478	399	353	203

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

V-HeFT Trial

AF has No Prognostic Significance



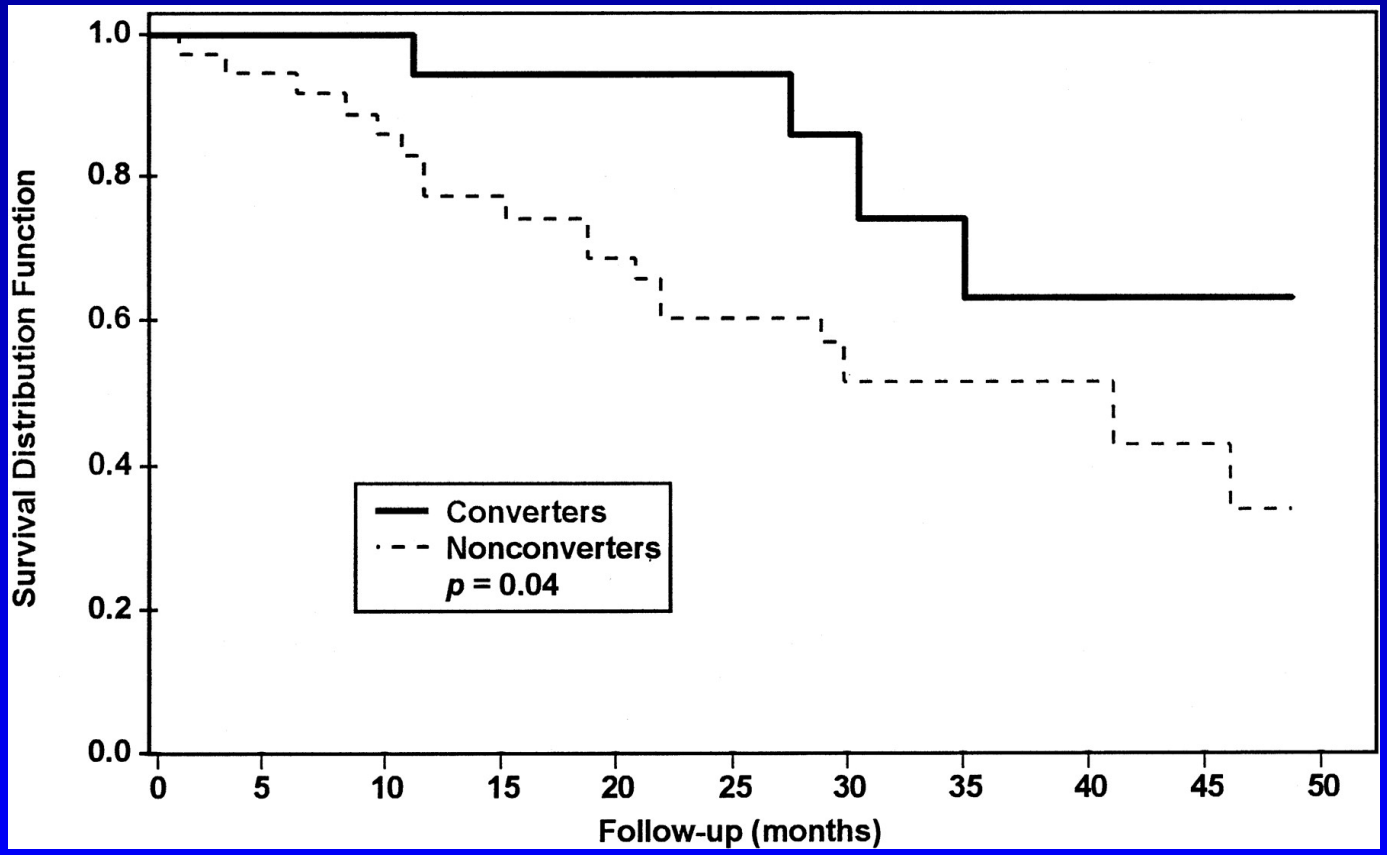
Carson P. Circulation. 1993;84 (suppl VI):VI-102–VI-110.

Does Maintaining Sinus Improve Outcomes of CHF?

Yes and No

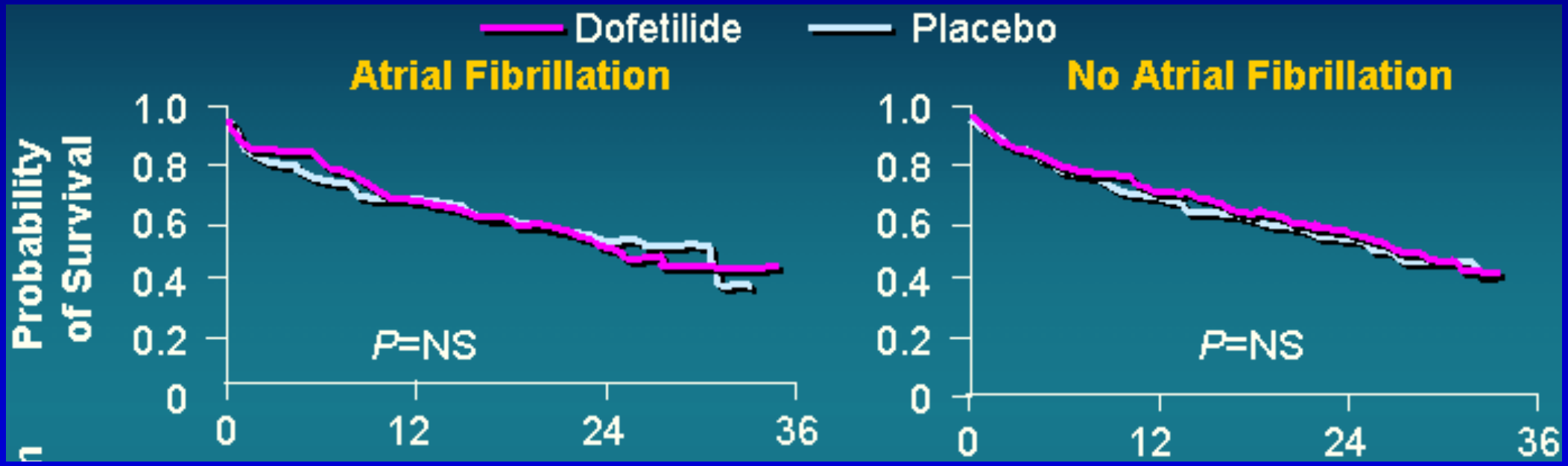
Yes: CHF-STAT Trial

Conversion on Amiodarone - Advantage



Deedwania PC. Circulation 1998;98:2574-9

No: DIAMOND CHF

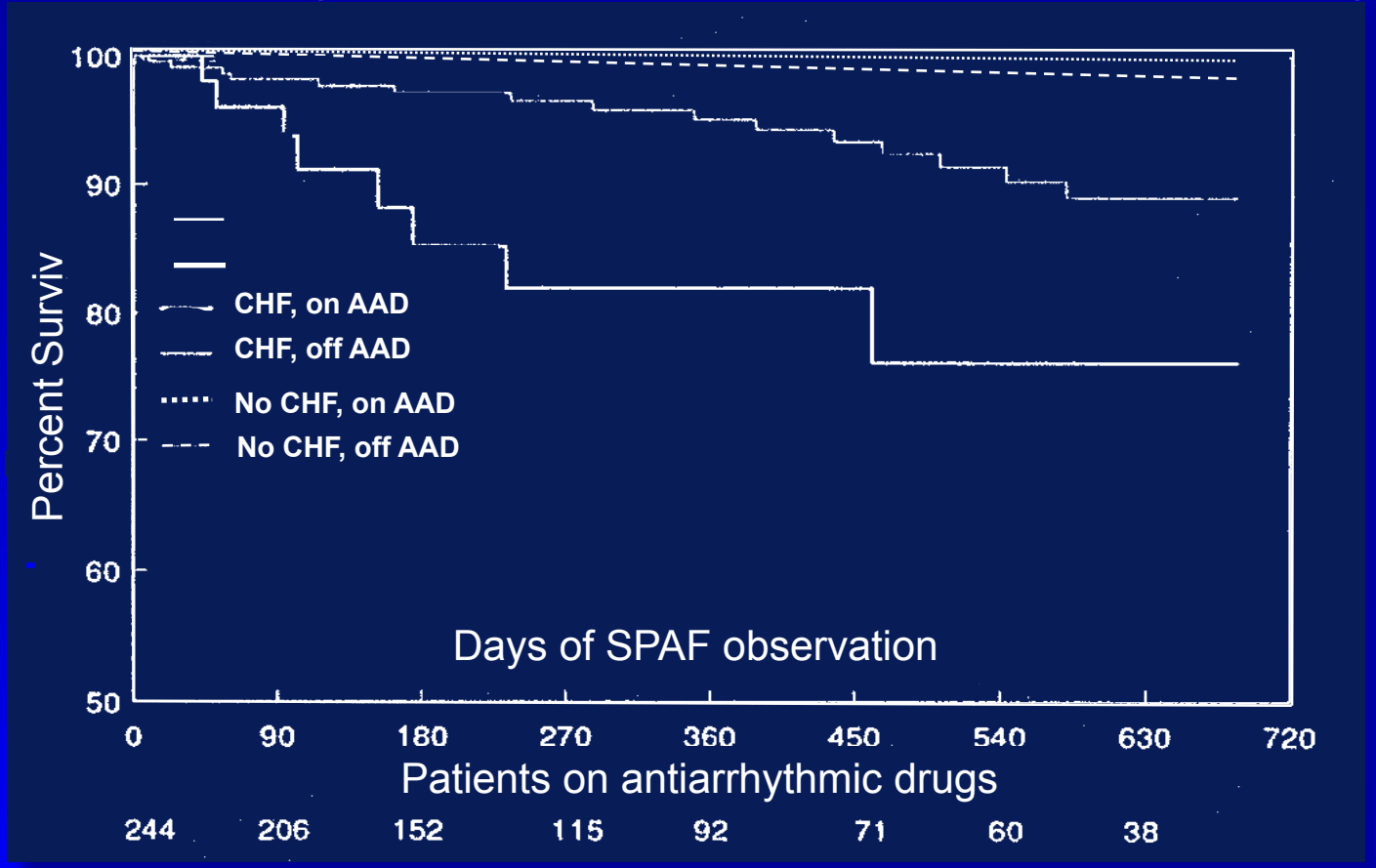


. . . but antiarrhythmics may not improve survival

Torp-Pedersen C. N Engl J Med 1999-341:857-865

No: The SPAF Trial

Antiarrhythmics Increase Mortality



Flaker G. J Am Coll Cardiol 1992:20:527-32

New Antiarrhythmic Drugs

Outcomes May be Drug Dependant

- Azimilide (Ikr/Iks)
- Dronedarone (de-iodinated amio)
- Tedisamil (Pan-K channel blockade)
- H345/52 (Ikr and ICA)
- SB 207266 (5-HT 4 receptor blocker)
- SB 237376 (K+ and Ca++ channel blocker)
- RSD 1235 (atrial selective, frequency-dependent block of Na+ and K+ currents)

Digoxin Bad, Sinus Rhythm Good?

Time-Dependent Survival in AFFIRM

Covariate	*P*-Value	Hazard Ratio	99% CI
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
Antiarrhythmic use	0.0005	1.49	1.11-2.01

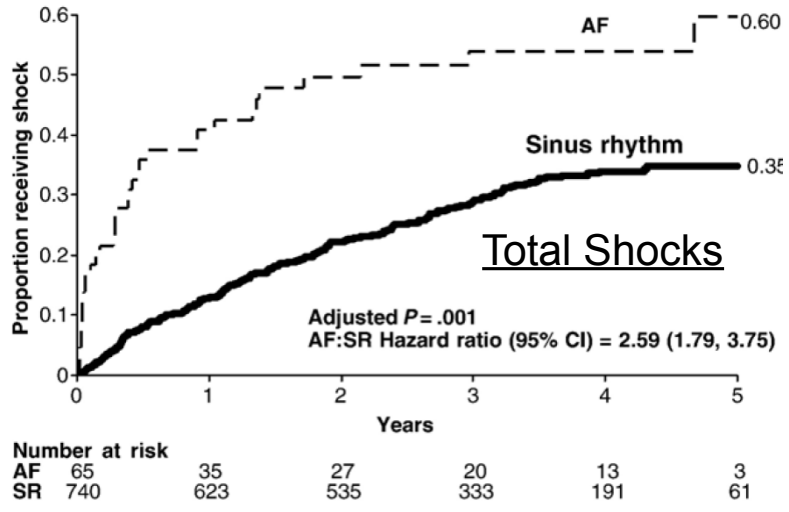
HR <1.00: decreased risk of death.

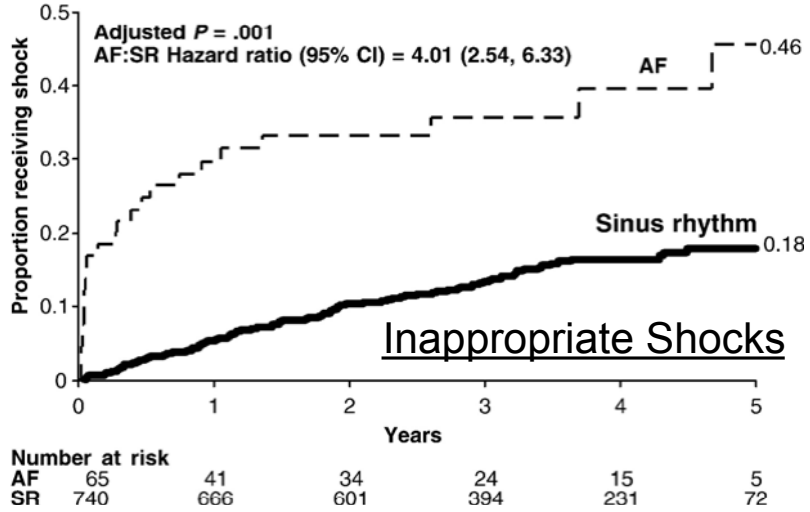
HR >1.00: increased risk of death.

AFFIRM Investigators. Circulation 2004;109:1509-1513

AF in SCD-HeFT

	Mortality		2.5-y KM Rate		HR (95% CI)
Patient Group	**AF**	**SR**	**AF**	**SR**	
All	37.0% (64)	25.4% (592)	25.5	16.4	1.02(0.76-1.37) p=0.98
Amiodarone	37.5% (24)	27.2% (210)	26.6	18.2	0.91(0.57-1.44)p=0.68
Placebo	36.4% (16)	28.3% (226)	22.7	18.0	0.94(0.53-1.64) p=0.82
ICD	36.9% (24)	20.6% (156)	26.3	13.9	1.25 (0.74-2.12) p=0.40





Singh SN. Am Heart J 2006;152:974

AF in CHF - Concerns

- Sicker patient – more severe CHF
- Less benefit from ICD
- Inappropriate ICD shocks
- Increased risk of death
- Difficult to manage

Management Depends on AF Type

- New onset
- Paroxysmal
- Persistent
- Permanent
- Unknown type and duration

AF in CHF – Management

- Anticoagulation – drugs and devices
- Rate control – drugs and ablation
- Rhythm control – drugs and ablation

Approach to Treatment

Any (or all) may apply

- Anticoagulation
- Rate control
- Rhythm control

$CHADS_2$ Risk Stratification

Risk Factors for Stroke		Score
C	Recent congestive heart failure	1
H	Hypertension	1
A	Age ≥ 75 (≥ *65 a risk also)*	1
D	Diabetes mellitus	1
S_2	History of stroke or transient ischemic attack	2

Annual risk - 2.6-5% in elderly (over age 65),
4-8% for one risk factor, 10-17% for two risk factors

Chugh. J Am Coll Cardiol. 2001;37:371-78

Rockson. J Am Coll Cardiol. 2004;43:929-935

Other Anticoagulants

No data support these in CHF

- Thrombin inhibitors
- Heparin
- Aspirin
- Clopidogrel
- Idraparinux

Anticoagulation – The Bottom Line

- Warfarin is no one's favorite drug but. . .
- Warfarin has no substitute

ACC/AHA/ESC Guidelines

Anticoagulation Strategies

Patient Features	Antithrombotic Therapy	Class of Recommendation
Age less than 60 y, no heart disease (lone AF)	Aspirin (81 to 325 mg per day) or no therapy	I
Age less than 60 y, heart disease but no risk factors*	Aspirin (81 to 325 mg per day)	I
Age 60 to 74 y, no risk factors*	Aspirin (81 to 325 mg per day)	I
Age 65 to 74 y with diabetes mellitus or CAD	Oral anticoagulation (INR 2.0 to 3.0)	I
Age 75 y or older, women	Oral anticoagulation (INR 2.0 to 3.0)	I
Age 75 y or older, men, no other risk factors	Oral anticoagulation (INR 2.0 to 3.0) or aspirin (81 to 325 mg per day)	I
Age 65 or older, heart failure	Oral anticoagulation (INR 2.0 to 3.0)	I
LV ejection fraction less than 35% or fractional shortening less than 25%, and hypertension	Oral anticoagulation (INR 2.0 to 3.0)	I
Rheumatic heart disease (mitral stenosis)	Oral anticoagulation (INR 2.0 to 3.0)	I
Prosthetic heart valves	Oral anticoagulation (INR 2.0 to 3.0 or higher)	I
Prior thromboembolism	Oral anticoagulation (INR 2.0 to 3.0 or higher)	I
Persistent atrial thrombus on TEE	Oral anticoagulation (INR 2.0 to 3.0 or higher)	IIa

Fuster V. J Am Coll Cardiol 2006;48:149-246

Anticoagulation in AF with CHF

The Future

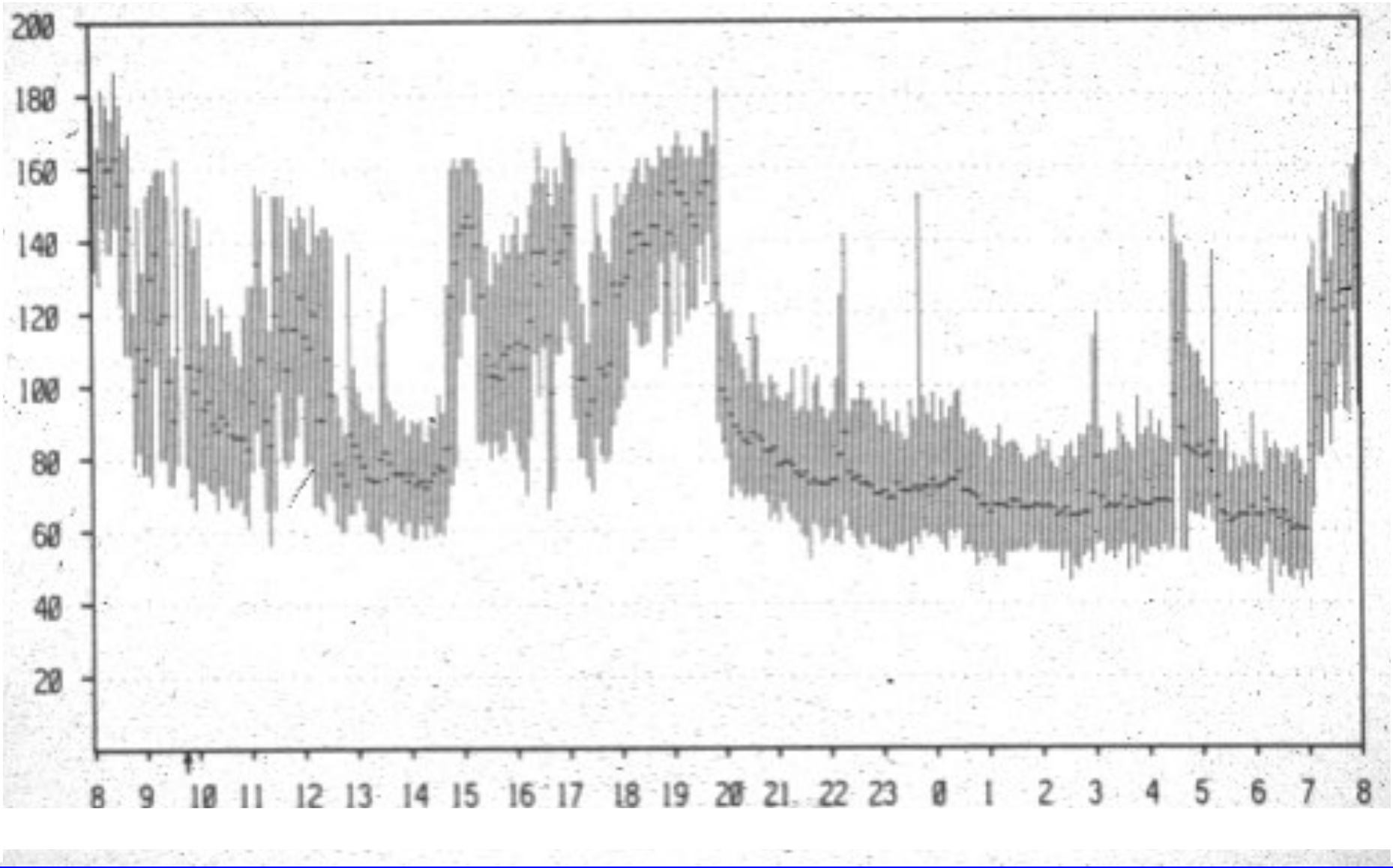
- Better selection of who to anticoagulate
- New thrombin inhibitors - maybe
- Atrial appendage occlusion devices
- Ablation (?)

Approach to Treatment

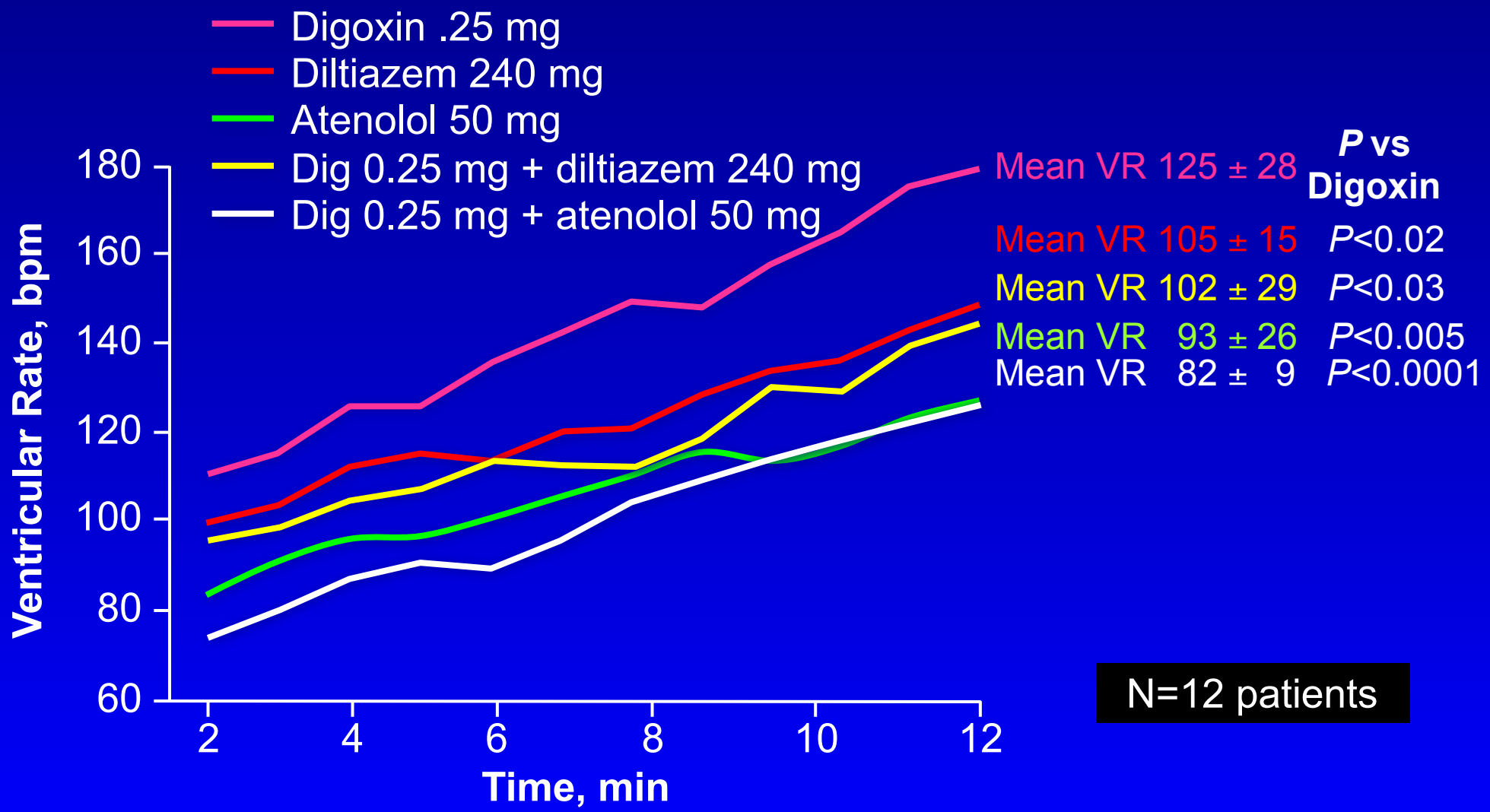
Any (or all) may apply

- Anticoagulation
- Rate control
- Rhythm control

AF – Heart Rate Variation



Rate Control of AF with Exercise



N=12 patients

Farshi R. J Am Coll Cardiol. 1999;33:304-310

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The Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study

Approaches to Control Rate in Atrial Fibrillation

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Iowa City, Iowa; New Haven, Connecticut; Los Angeles, Sacramento, San Diego, and Irvine, California; Washington, DC; Rochester, New York; and Seattle, Washington

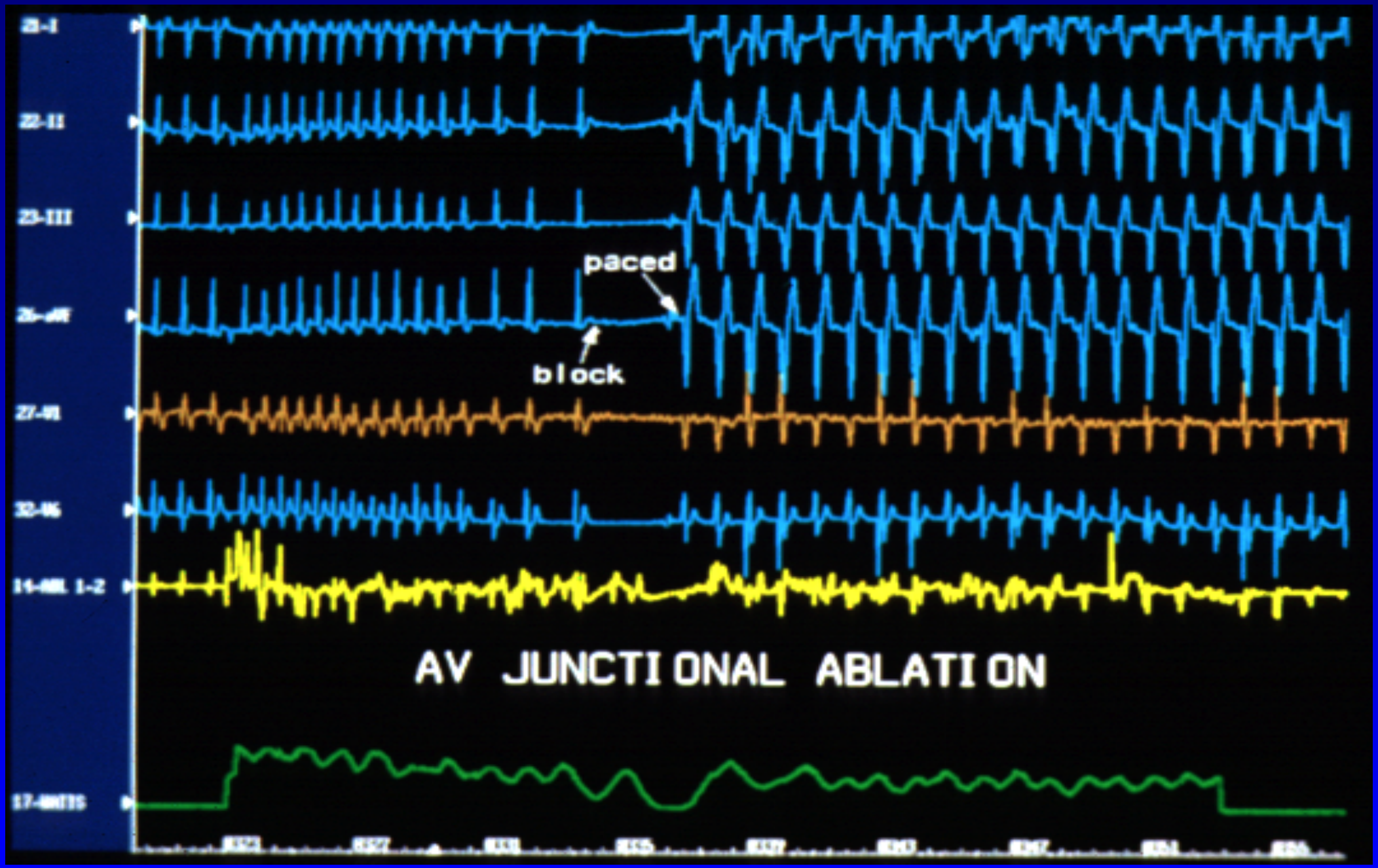
OBJECTIVES We sought to evaluate approaches used to control rate, the effectiveness of rate control, and switches from one drug class to another in the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study.

BACKGROUND The AFFIRM study showed that atrial fibrillation (AF) can be treated effectively with rate control and anticoagulation, but drug efficacy to control rate remains uncertain.

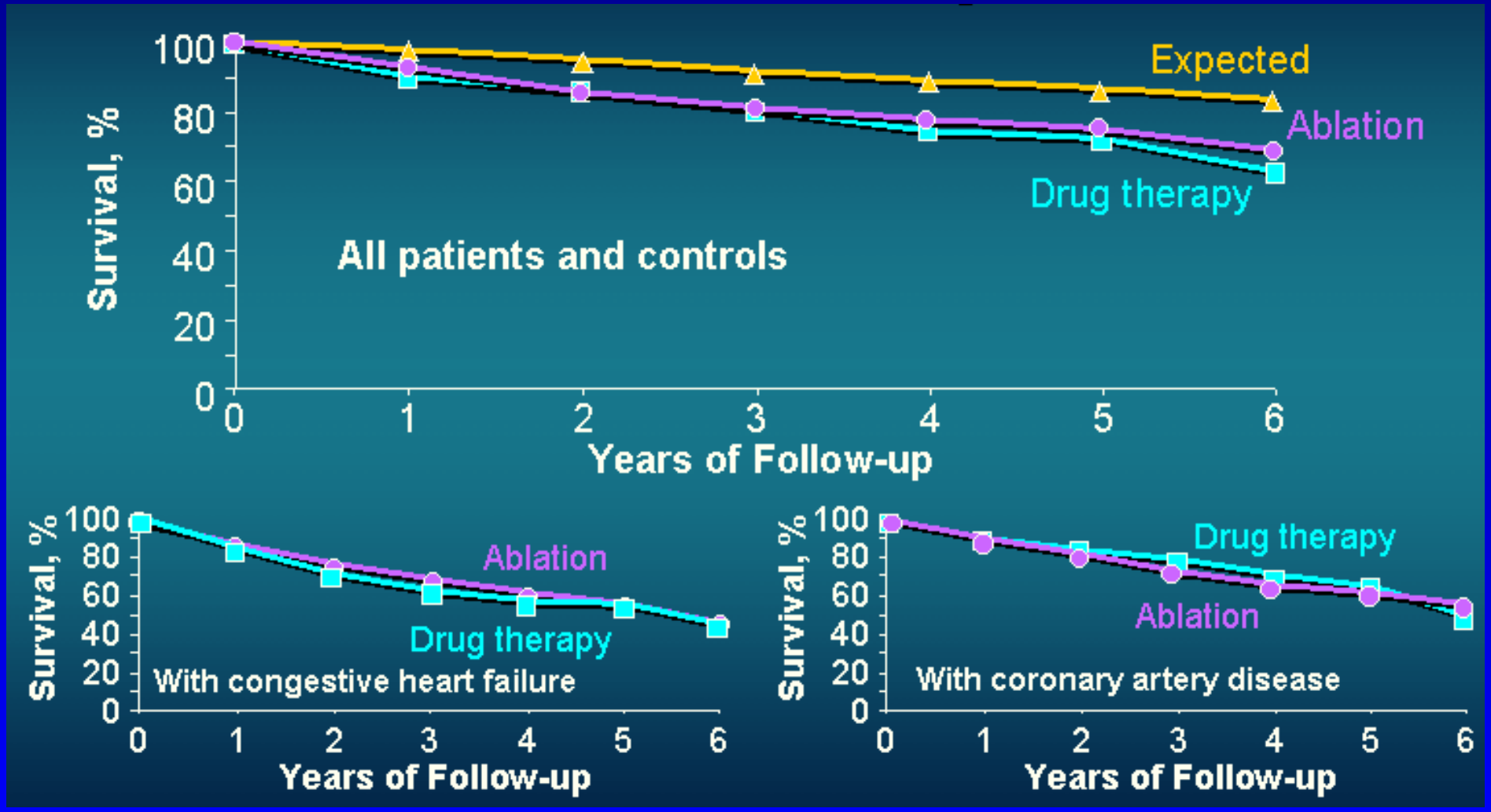
METHODS Patients (n = 2,027) randomized to rate control in the AFFIRM study were given rate-controlling drugs by their treating physicians. Standardized rate-control efficacy criteria developed a priori included resting heart rate and 6-min walk tests and/or ambulatory electrocardiographic results.

RESULTS Average follow-up was 3.5 ± 1.3 years. Initial treatment included a beta-adrenergic blocker (beta-blocker) alone in 24%, a calcium channel blocker alone in 17%, digoxin alone in 16%, a beta-blocker and digoxin in 14%, or a calcium channel blocker and digoxin in 14% of patients. Overall rate control was achieved in 70% of patients given beta-blockers as the first drug (with or without digoxin), 54% with calcium channel blockers (with or without digoxin), and 58% with digoxin alone. Adequate overall rate control was achieved in 58% of patients with the first drug or combination. Multivariate analysis revealed an association between first drug class and several clinical variables. There were more changes to beta-blockers than to the other two-drug classes ($p < 0.0001$).

CONCLUSIONS Rate control in AF is possible in the majority of patients with AF. Beta-blockers were the most effective drugs. To achieve the goal of adequate rate control in all patients, frequent medication changes and drug combinations were needed. (J Am Coll Cardiol 2004;43: 000–000) © 2004 by the American College of Cardiology Foundation


paced
block
AV JUNCTIONAL ABLATION

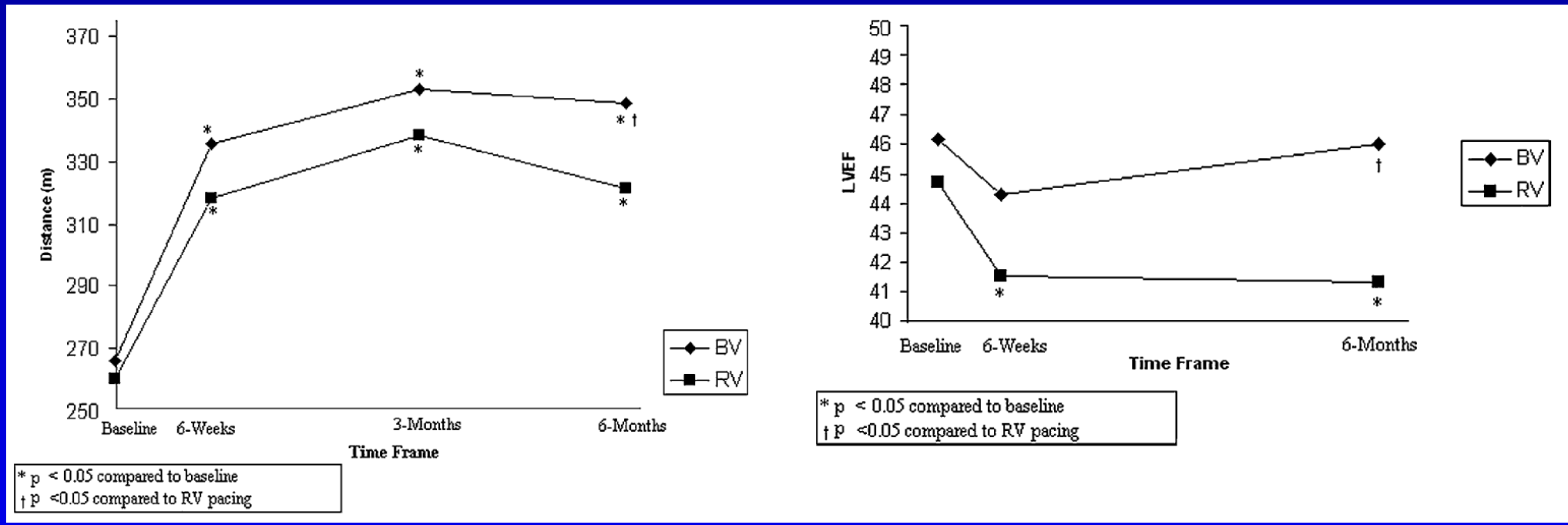
AV Junctional Ablation



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

AV Junctional Ablation

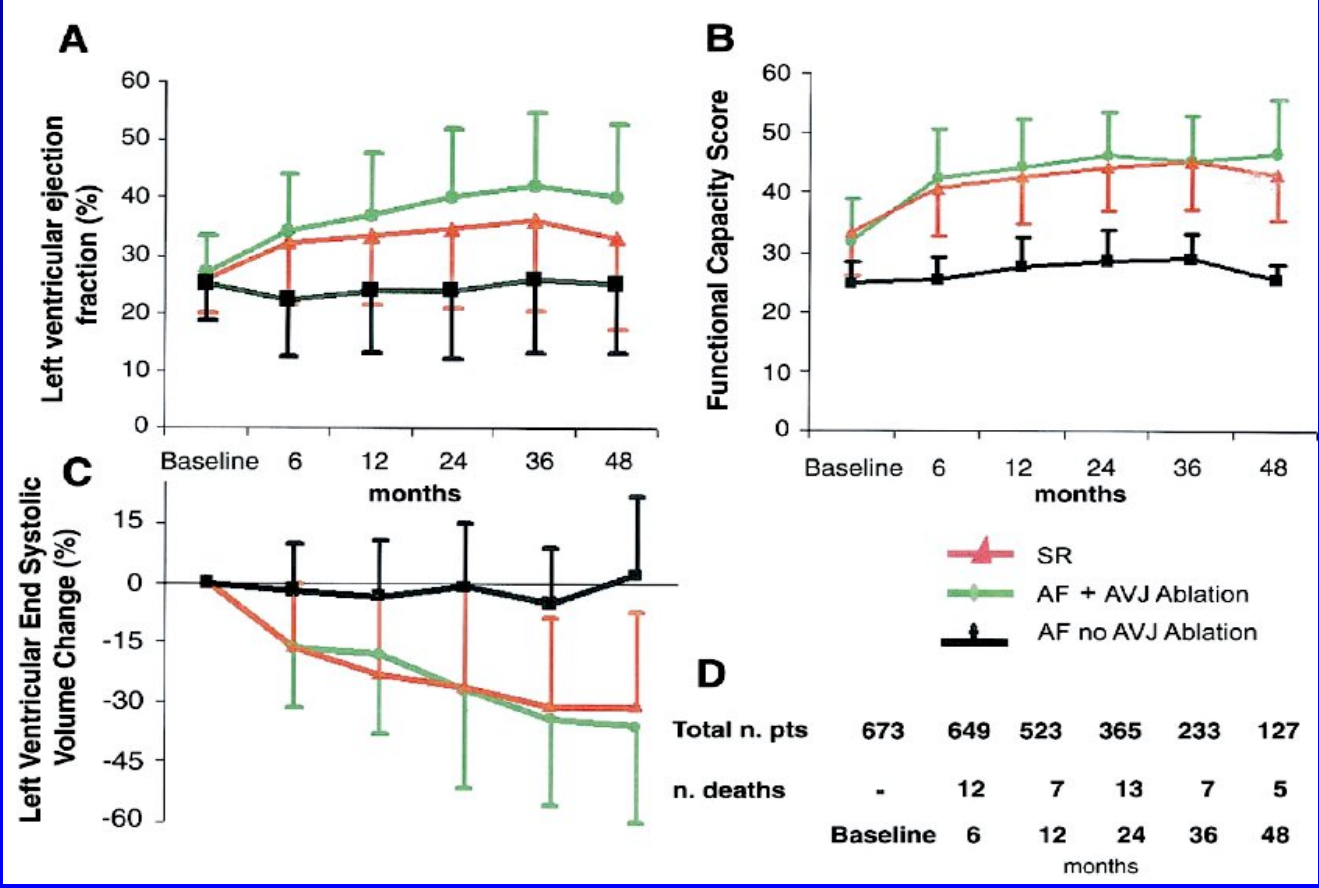
BiV, VVI, DDD?



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

CRT Works in Atrial Fibrillation

But AV Junctional Ablation May Be Needed



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

Approach to Treatment

Any (or all) may apply

- Anticoagulation
- Ventricular rate control
- Rhythm control

Outpatient cardioversion of atrial arrhythmias: Efficacy, safety, and costs

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Background Outpatient direct current (DC) cardioversion is performed routinely, yet scant data support this approach. We studied the efficacy, safety, and costs of outpatient cardioversion.

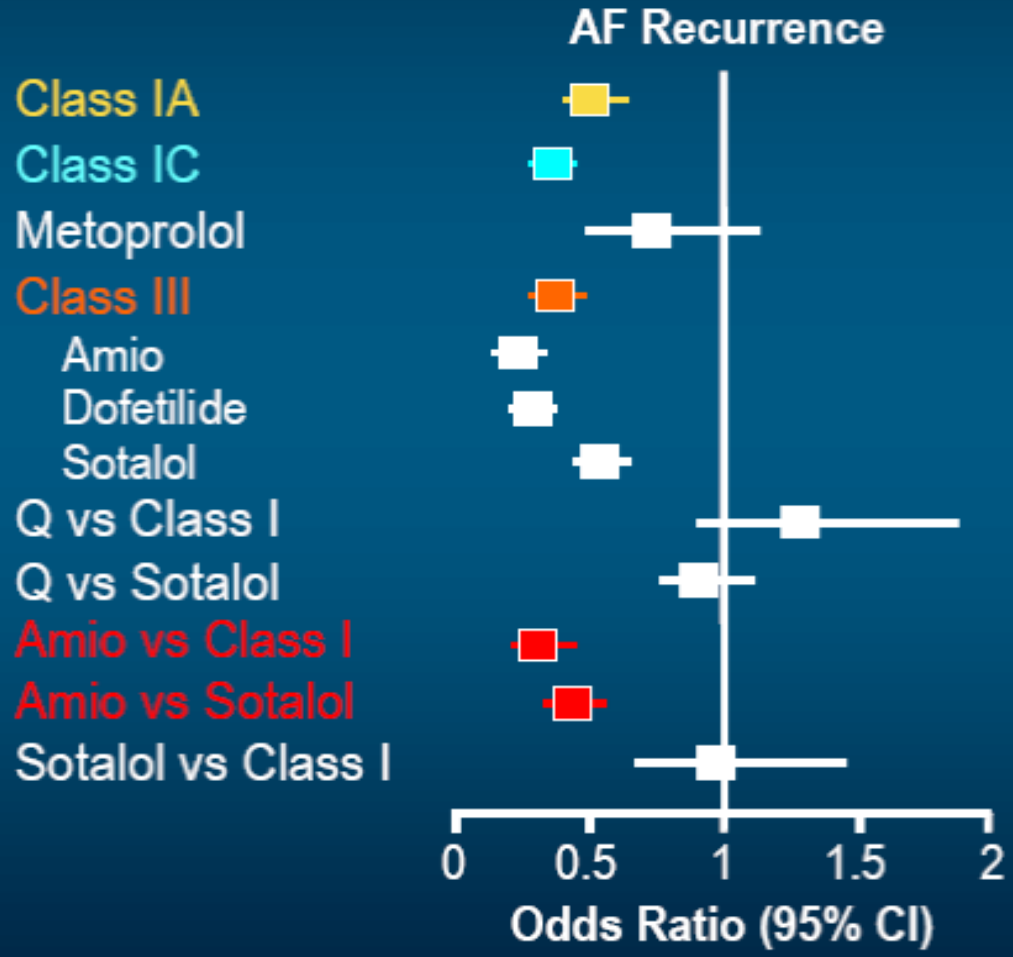
Methods A retrospective analysis of outpatient cardioversions was performed in a 5-year period at an academic medical center in 532 consecutive outpatients with an atrial tachyarrhythmia. The protocol included anticoagulation (international normalized ratio ≥2.0) for ≥4 consecutive weekly draws and then DC cardioversion with the patient under intravenous anesthesia. Arrhythmia symptoms, antiarrhythmic therapy use, and costs were evaluated.

Results Ninety percent of patients were discharged in sinus rhythm after cardioversion with a median number of shocks of 1 (range, 1-6) for atrial flutter (n = 113), atrial tachycardia (n = 13), and atrial fibrillation (n = 406). Sixty-seven percent of patients were treated with an antiarrhythmic drug. The complication rate was 2.6%, with 11 unplanned admissions. Thromboemboli occurred only in patients whose anticoagulation deviated from protocol and included chronic hemianopsia starting 4 days after cardioversion, transient right-sided weakness, and cerebral vascular accident 3 days after cardioversion, despite negative results on a transesophageal echocardiogram. Two patients had postcardioversion pulmonary edema. Bradycardia developed in 4 patients; transient pacemaker noncapture after the shock occurred in 4 patients. Transient postshock rhythms also included AV nodal Wenckebach and junctional rhythm. One patient had aspiration pneumonia. The mean cost of cardioversion was $464. Fees for anesthesia ranged from $525 to $650. The anesthetic costs ranged from $2.84 to $21.47. The cardiology fee averaged $501.

Conclusion Outpatient cardioversion is a low risk, effective, and economical procedure. (Am Heart J 2003;145: 233-8.)

Drugs to Prevent AF after Cardioversion – A Systematic Review

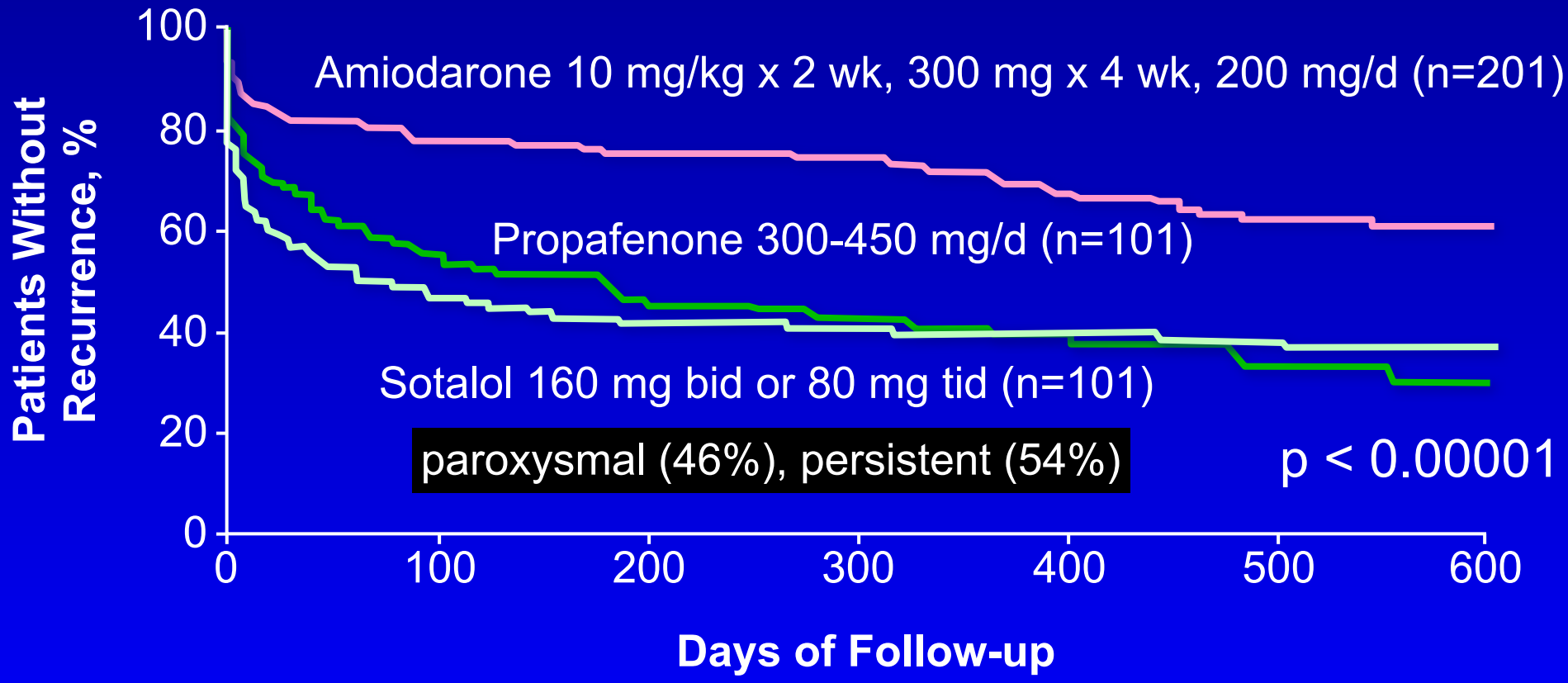
RCT Included Into Analysis	
Total	44
No. of patients	11,322
Placebo controlled	25
Active comparator	14
Persistent AF	38 (60% pts)
PAF/recent onset	6
EF >50%	41
Lone AF	1
Follow-up	1 year



Lafuente-Lafuente et al. *Arch Intern Med*. 2006;166:719-728.

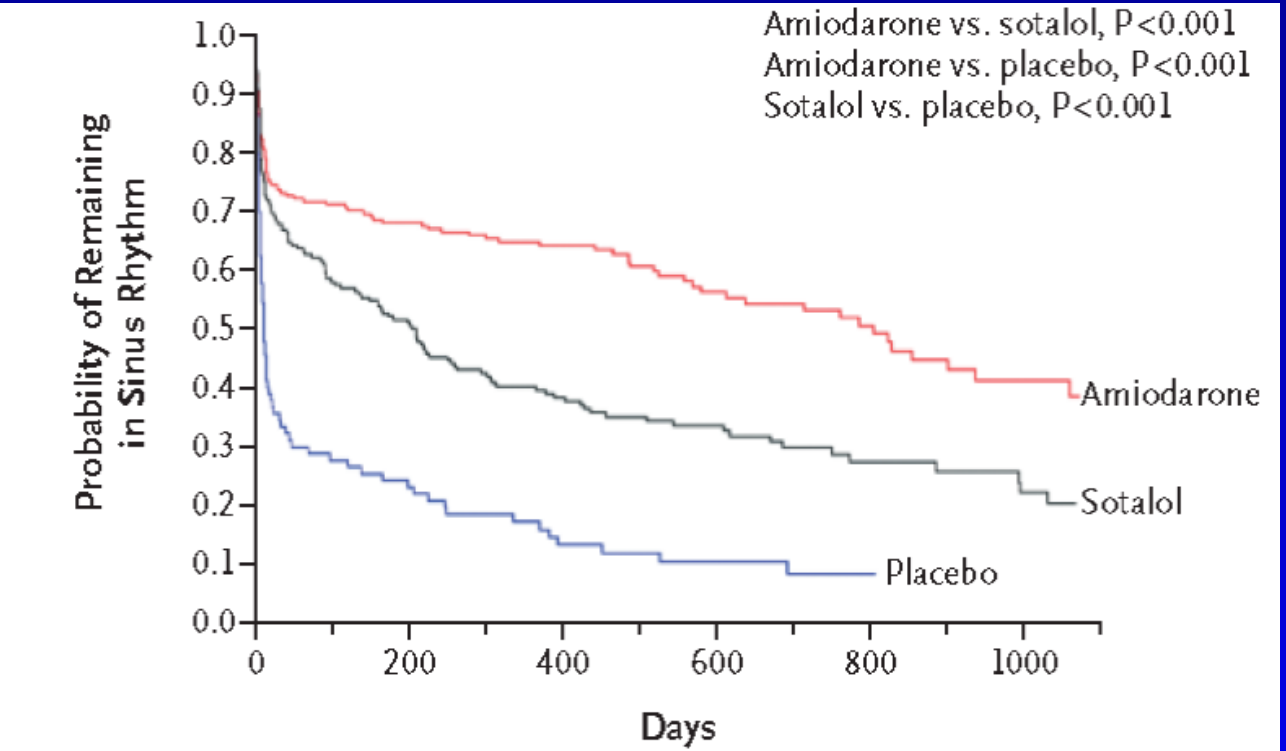
Amiodarone for Sinus Rhythm

CTAF (Canadian Trial of Atrial Fibrillation)



Roy D. N Engl J Med. 2000;342:913-920

SAFE-T Amiodarone vs. Sotalol



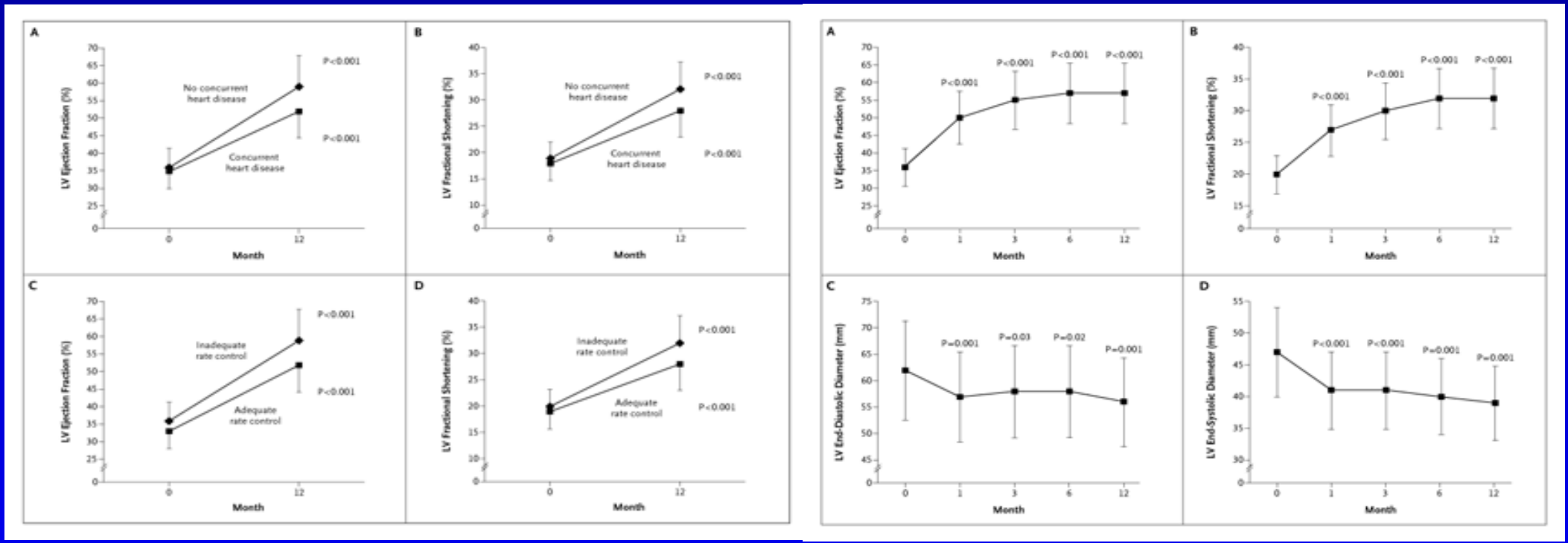
No. at Risk

Amiodarone	206	131	98	60	38	18
Sotalol	195	97	61	38	21	13
Placebo	90	21	11	8	5	2

Singh B. N Engl J Med. 2005;352:1861-1872

AF Ablation in CHF

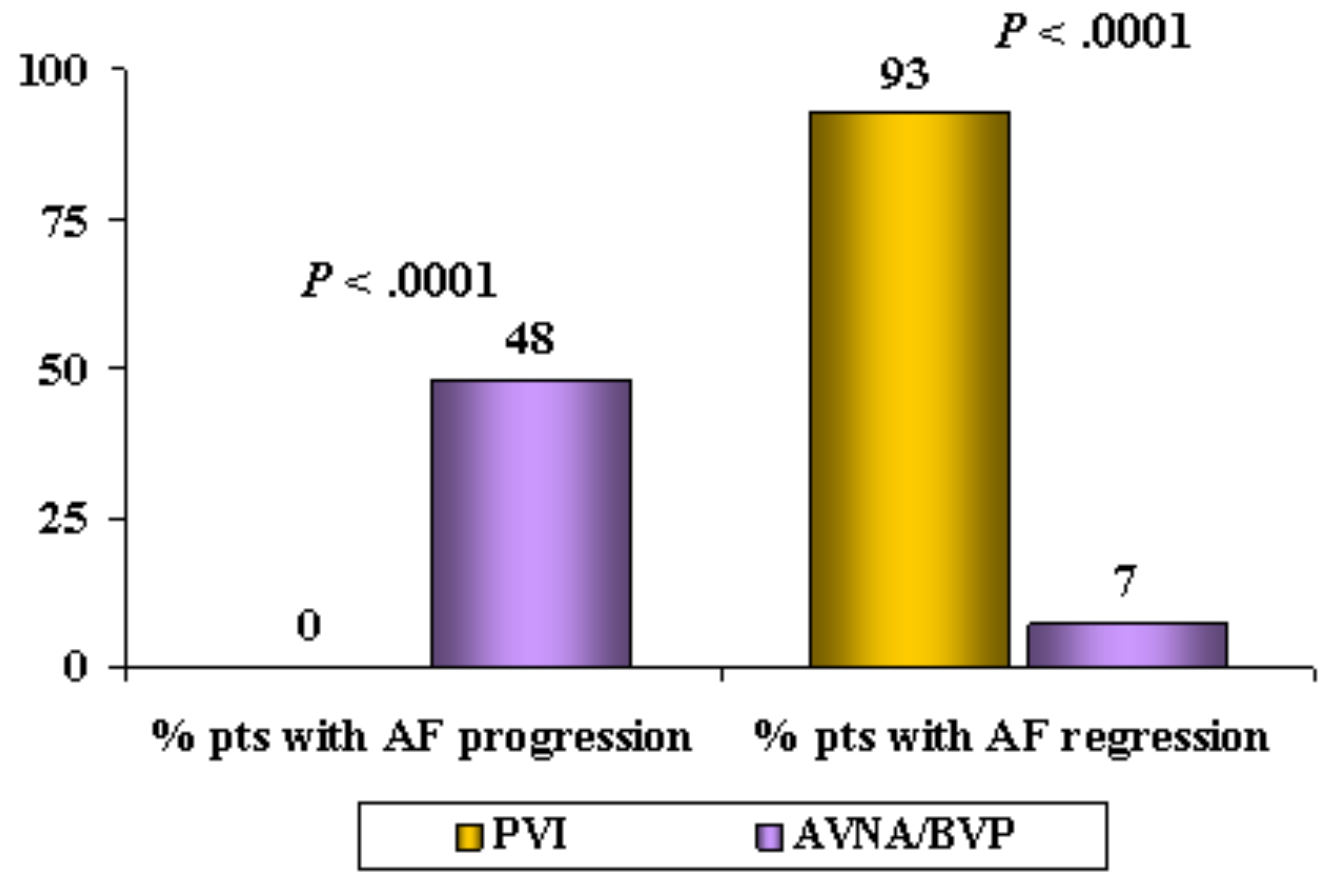
Improved Markers of Ventricular Function



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

PABA CHF

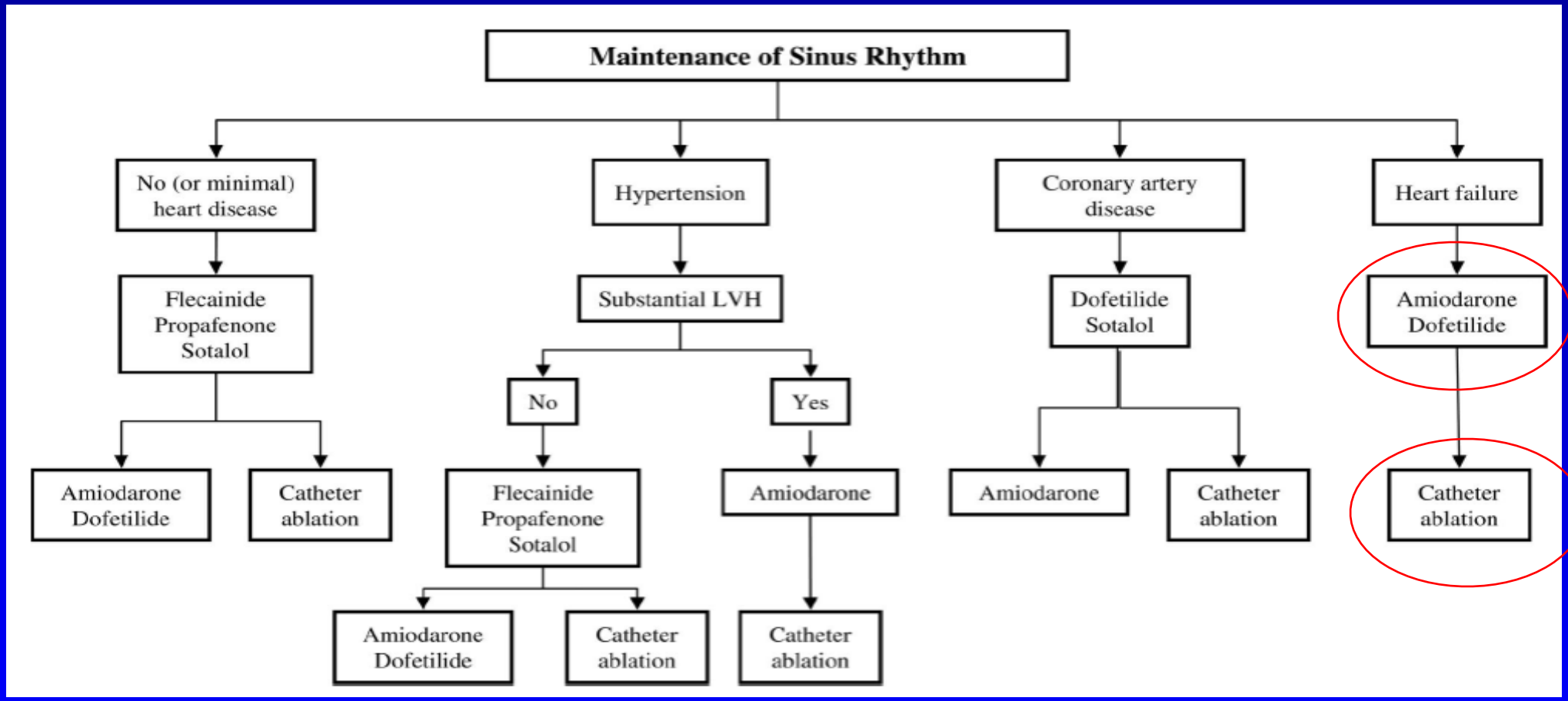
PV isolation vs. AVJ ablation/BiV pacing for AF in CHF



Khan MN, Heart Rhythm. 2006(3 Suppl):1S

ACC/AHA/ESC 2006 Guidelines

Rhythm Control – Recommendations



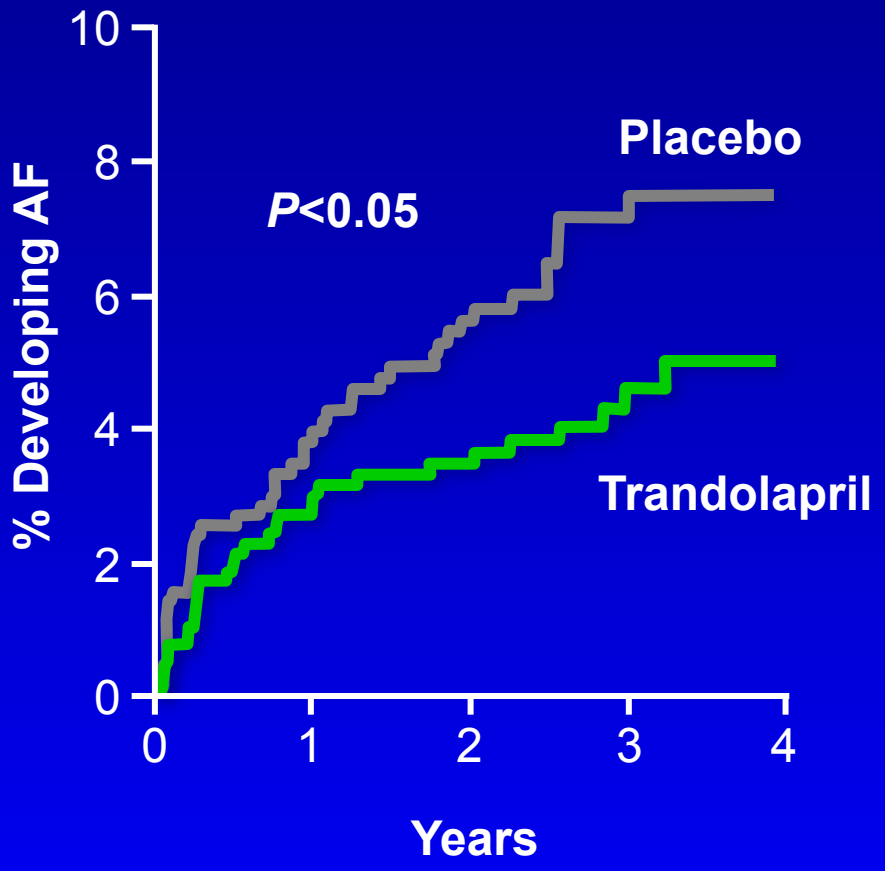
Fuster V. J Am Coll Cardiol. 2006;48:149-246

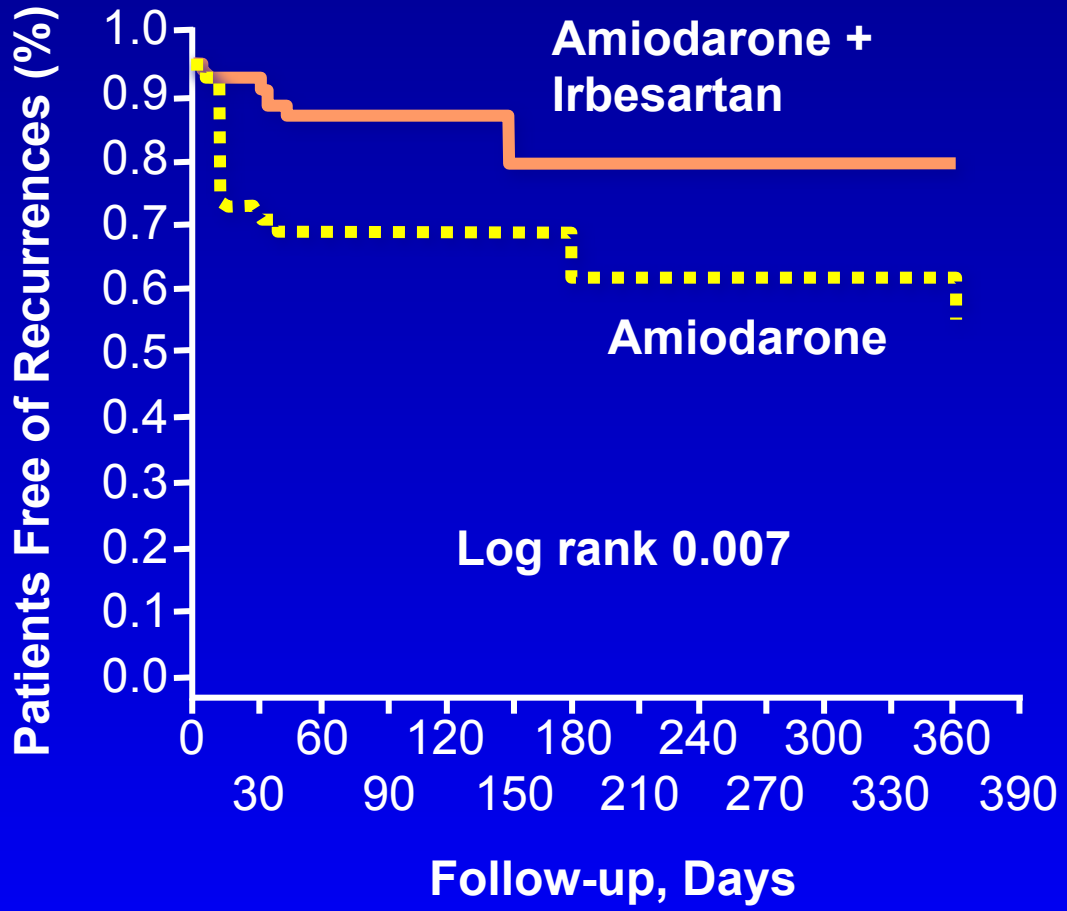
Novel Therapies for AF

None proven for AF in CHF

- ACE inhibitors/ARBs
- Fish oil
- Statins

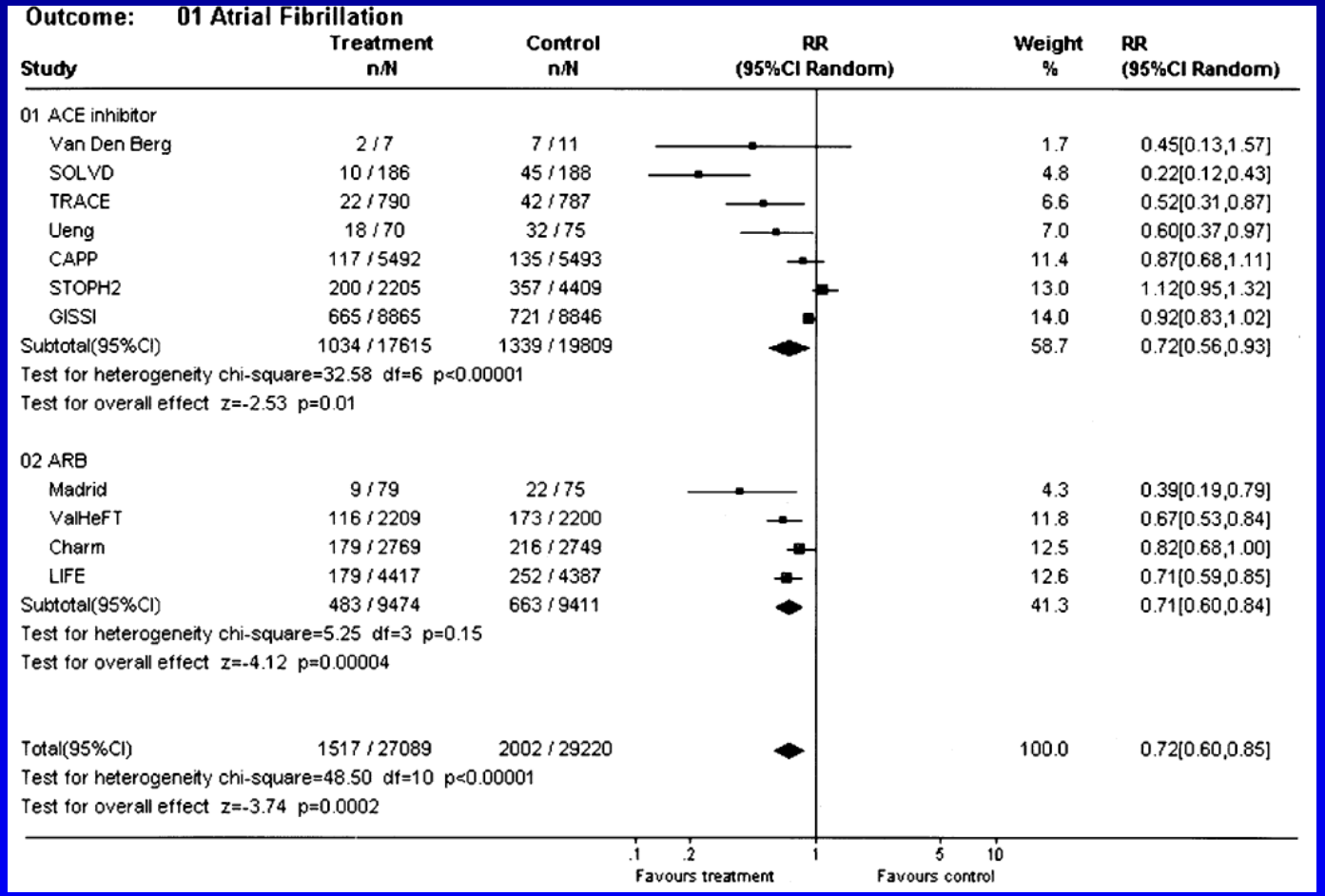
ACEI/ARB - Effect on AF





Pedersen OD. Circulation 1999;100:376-380
Madrid AH. Circulation 2002;106:331-336

ACEIs and ARBs for AF



Healey JS. J Am Coll Cardiol 2005;45:1832-9

Rhythm or 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

What about in patients with CHF?

AF-CHF Trial

- 1376 patients followed ≥2 years, 123 sites
- CHF, NYHA FC II-IV or LVEF ≤0.35 or prior hospitalization for CHF and LVEF ≤0.25
- 2/3's had persistent AF, >50% hospitalized for AF or CHF, generally stabilized

AF-CHF Trial

Results

- Mortality, CHF, stroke similar - rate vs rhythm
- 21% crossed from rhythm to rate and 10% crossed from rate to rhythm
- More in rhythm group hospitalized (46% vs 39%, p=0.0063) mainly due to AF and bradycardia (8.5% vs 4.9%), p= 0.0074
- Cardioversion more - rhythm group (39% vs 8%)

Typical Day at the Office

What We Have Learned

- 75 year old female, CHF (NYHA FC II), non-ischemic cardiomyopathy (EF = 0.30), s/p DDD ICD, has recent ICD shocks
- BP: 144/94, P 120, irregular
  - heart: S1, S2, S3
- EKG – LBBB, atrial fibrillation

AF and CHF in 2008

Bottom Line for the Average Patient

- Rate control/anticoagulation – an acceptable approach
- Rhythm control – for those with intolerable symptoms. New drugs are being developed.
- Ablation - rapid progress with hope for a cure