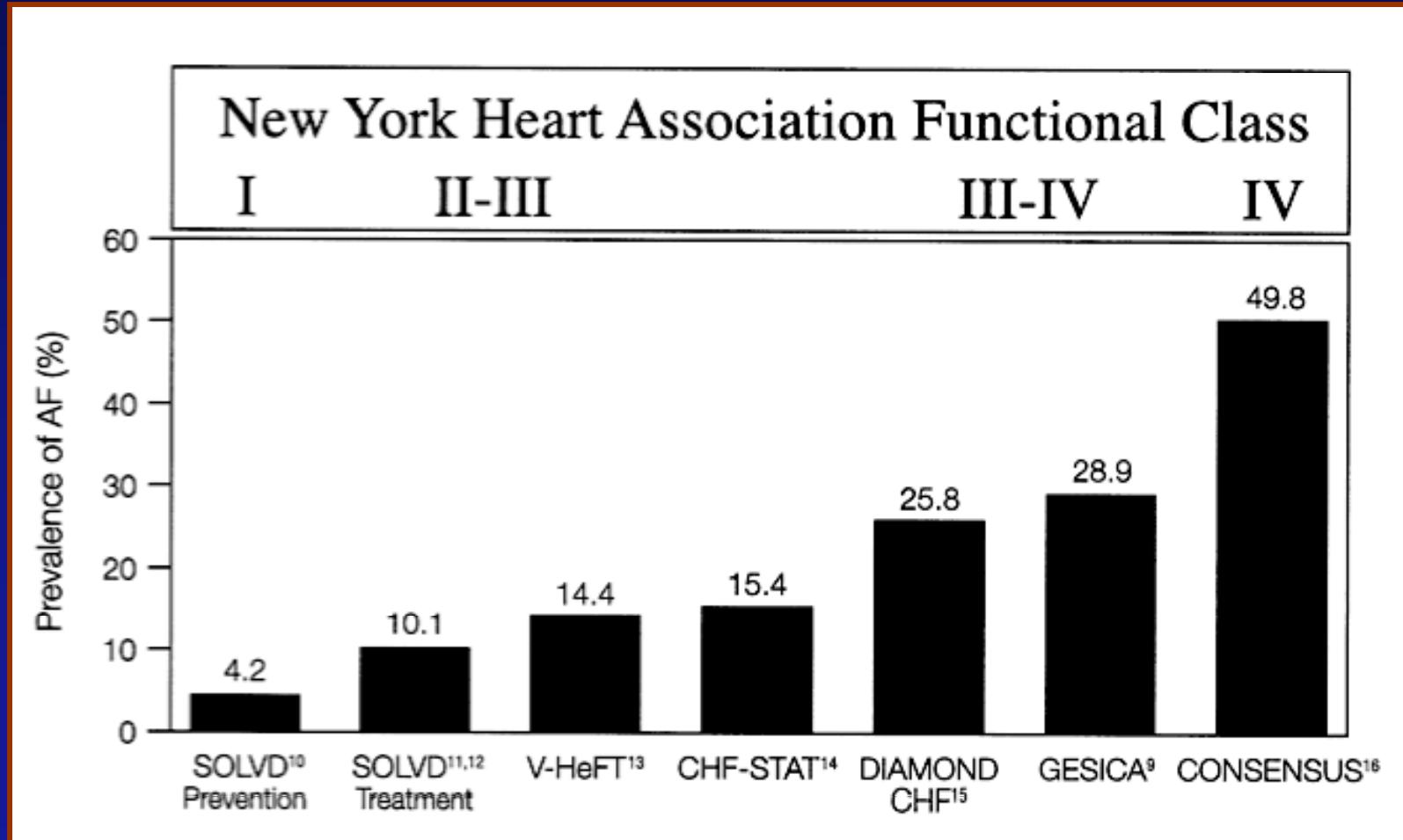


Heart Failure and Atrial Fibrillation: a Deadly Combination

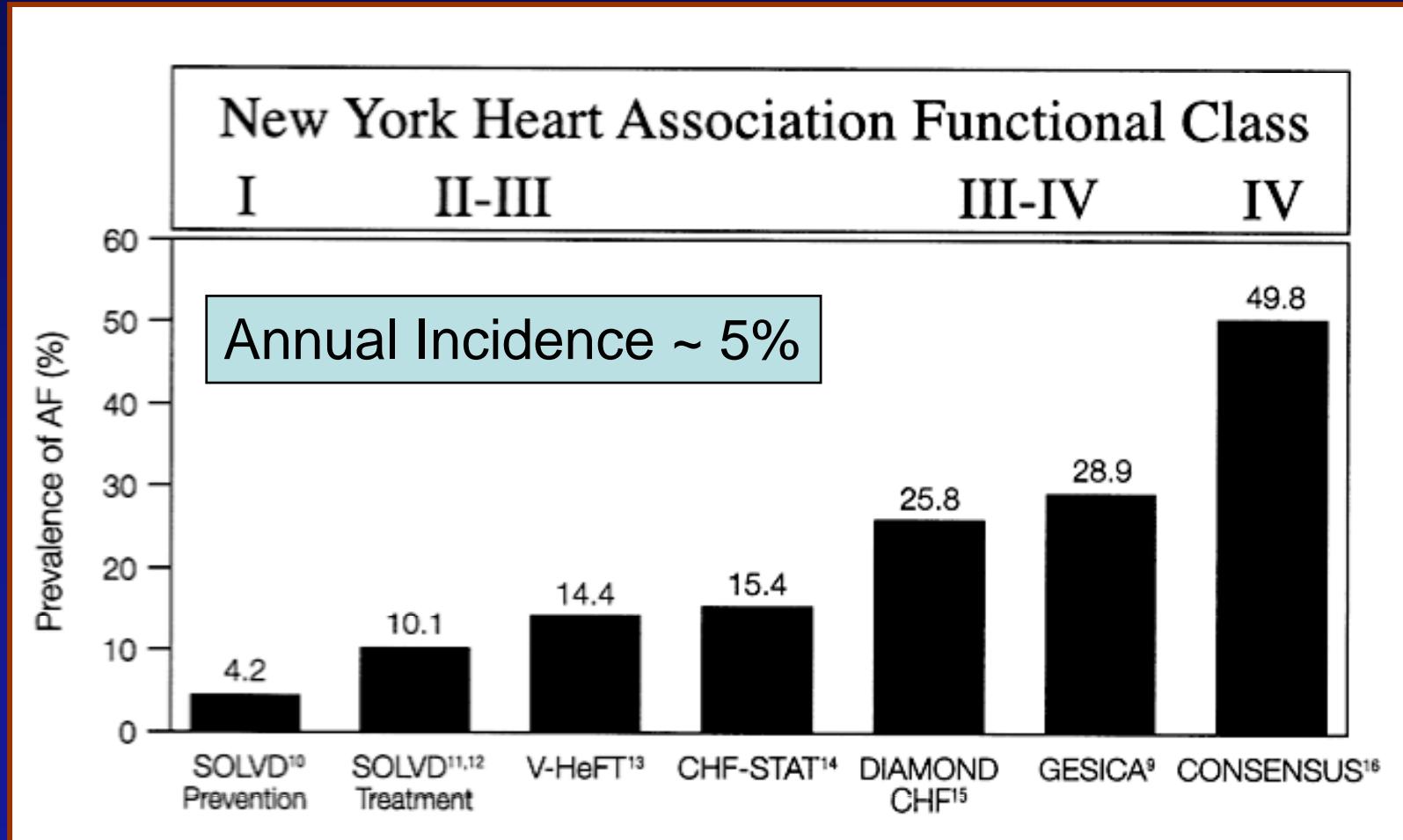
Jonathan S. Steinberg, MD
St. Luke's-Roosevelt Hospital Center
Columbia University
New York, NY

Prevalence of AF in Heart Failure



From Maisel and Stevenson, AJC 2003

Prevalence of AF in Heart Failure



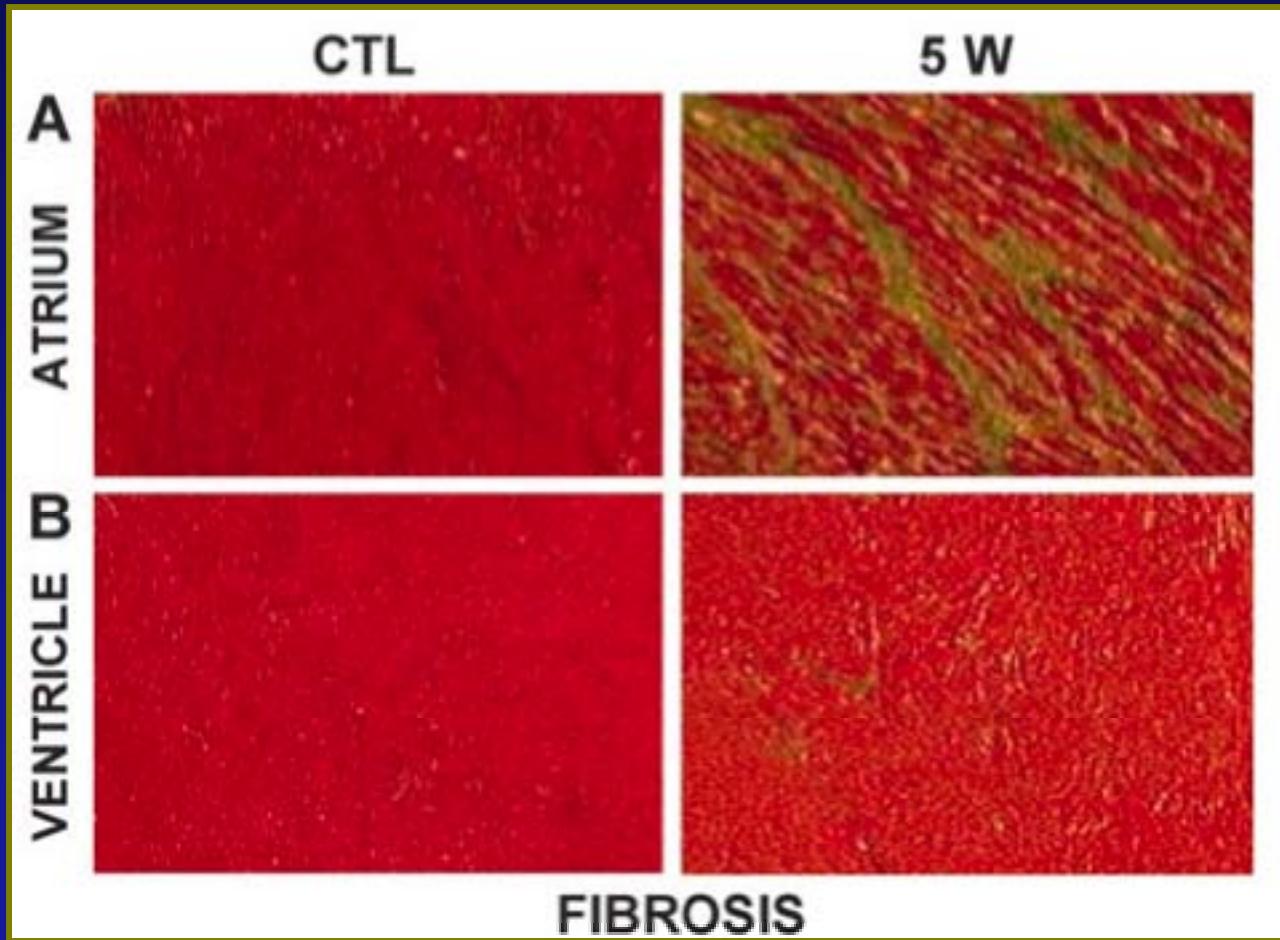
From Maisel and Stevenson, AJC 2003

Predictors of AF in Heart Failure

Prospective study of 344 patients in NSR followed for 19 mos; AF incidence = 5.2% and associated with clinical and hemodynamic deterioration and higher stroke and death rates.

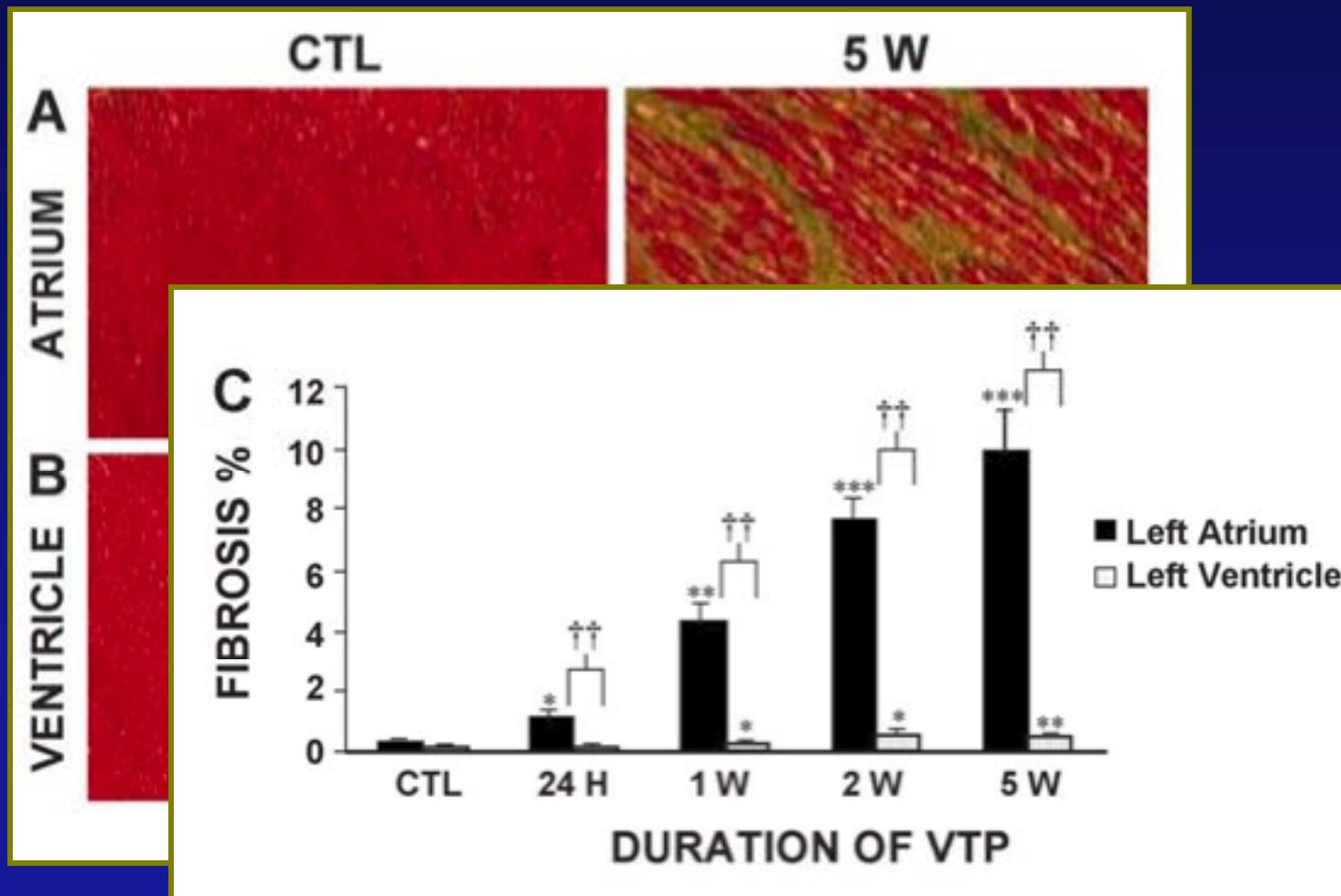
- Development of chronic AF
 - No factor identified
 - Including LA dimensions, volume, pressure
 - Including HF status and parameters
- Development of late chronic AF
 - Prior history of reversible AF
 - Reduced LA contribution to filling (atrial myopathy)

Atrial Remodeling in Heart Failure



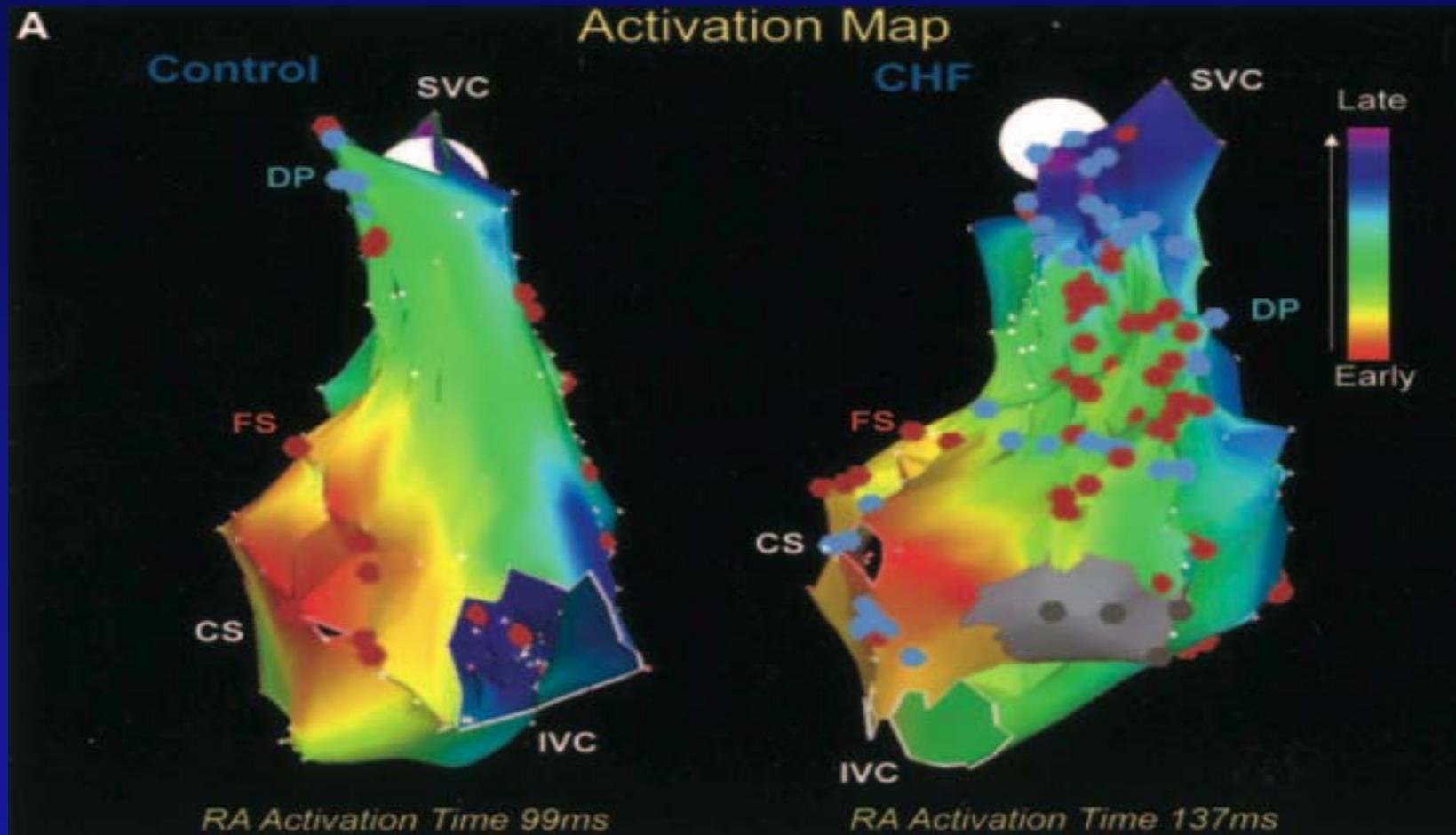
From Hanna et al, Cardiovasc Res 2004

Atrial Remodeling in Heart Failure



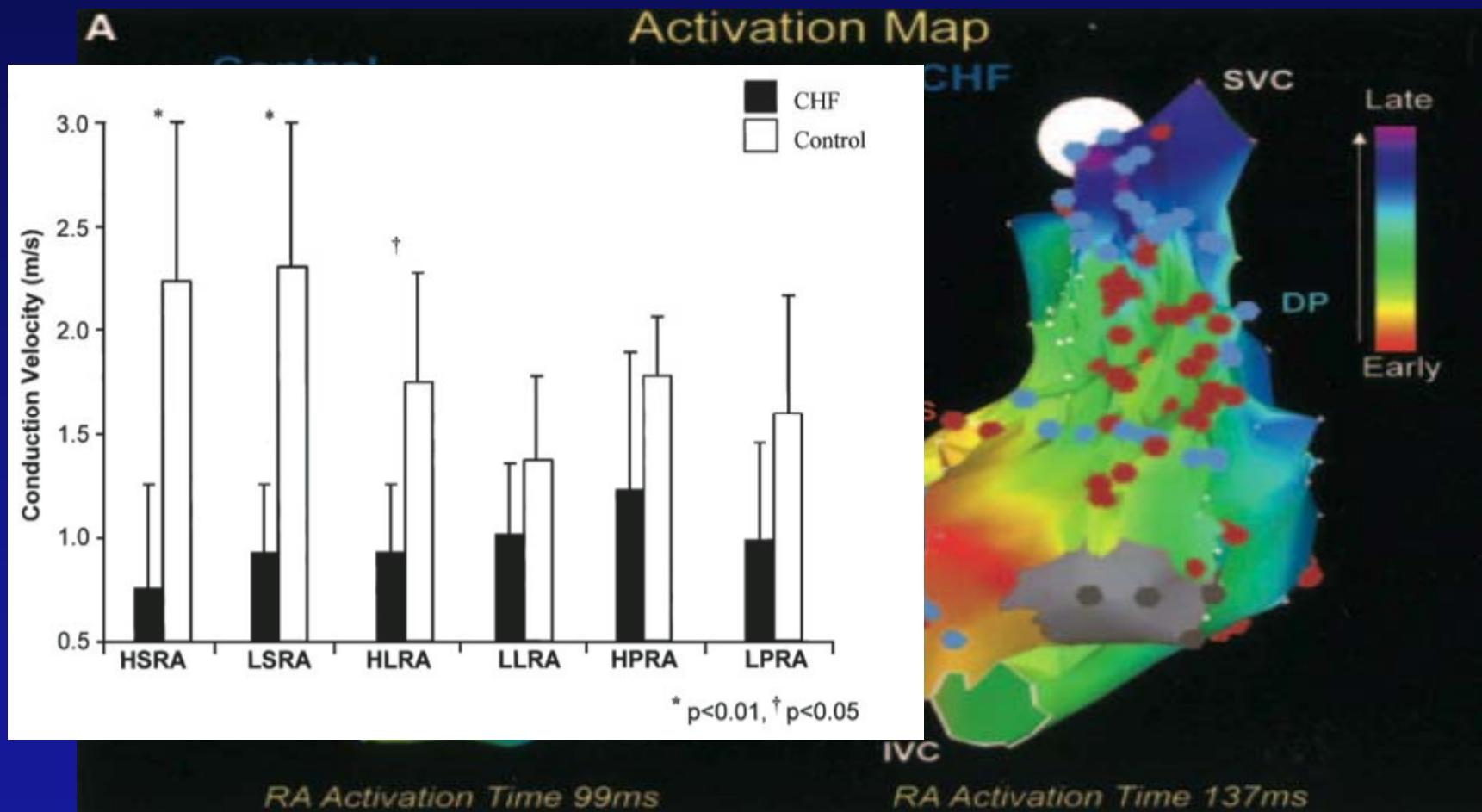
From Hanna et al, Cardiovasc Res 2004

Electrophysiologic Remodeling in Heart Failure



From Sanders et al, Circulation 20

Electrophysiologic Remodeling in Heart Failure



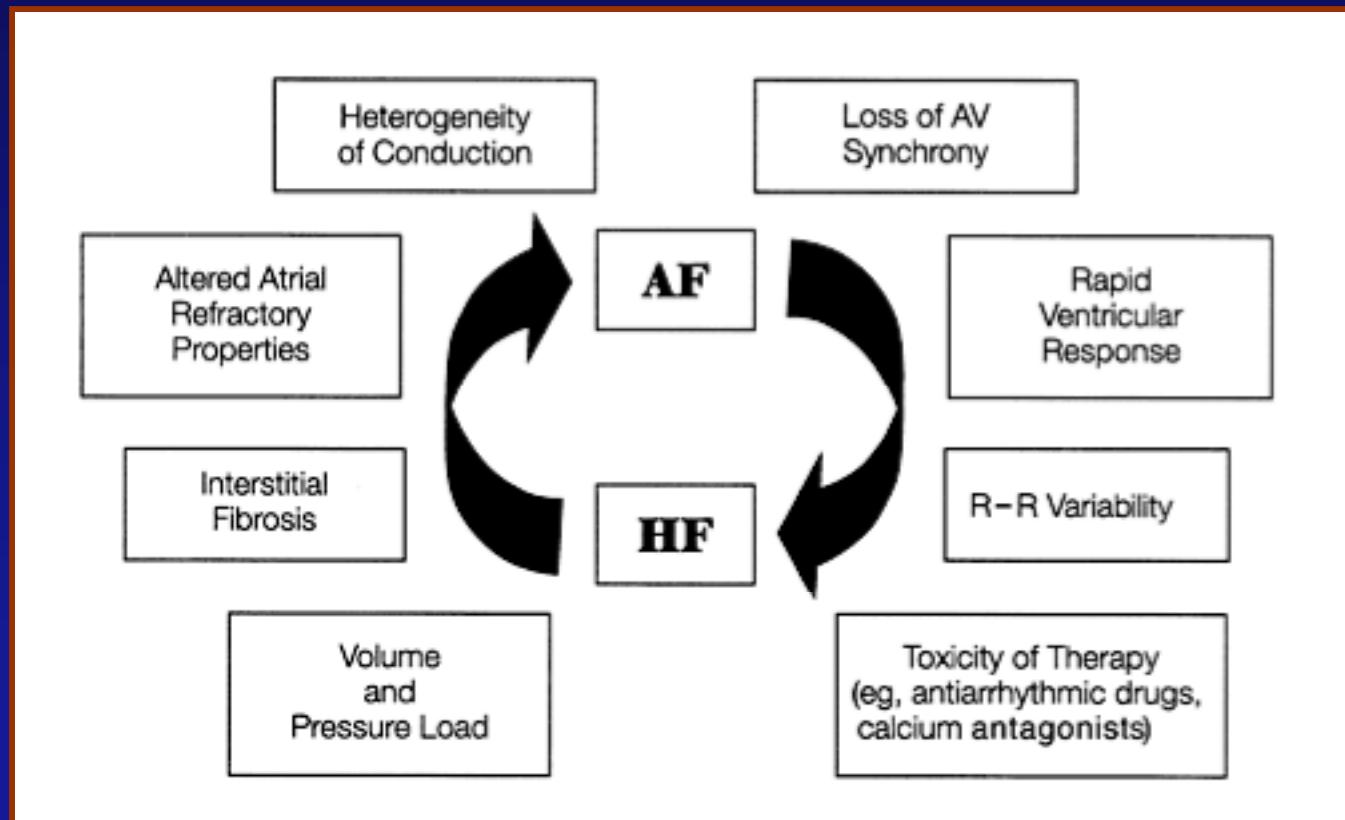
From Sanders et al, Circulation 2003

Pathology and Electrophysiology of AF in Heart Failure

- Pathology and Pathophysiology
 - White cell infiltration
 - Apoptosis
 - Increased collagen synthesis and fibrosis
 - Hypertrophy and chamber enlargement
 - Sympathetic and renin-angiotensin systems activation
 - Increased synthesis and activation of variety of maladaptive proteins and enzymes
 - Altered ion channel function
- Electrophysiology
 - Slow conduction
 - Abnormal sinus node function
 - Shortened and heterogenous atrial refractory periods
 - Increased automaticity and triggered activity

Hanna et al, Cardiovasc Res 2004; Sanders et al, Circulation 2003; Khan et al JACC 2004; Boixel et al, JACC 2003; Li et al, Circulation 1999; Yu et al, JACC 1997

Heart Failure and AF: Vicious Cycle



Interaction of AF and HF: Impact on Mortality

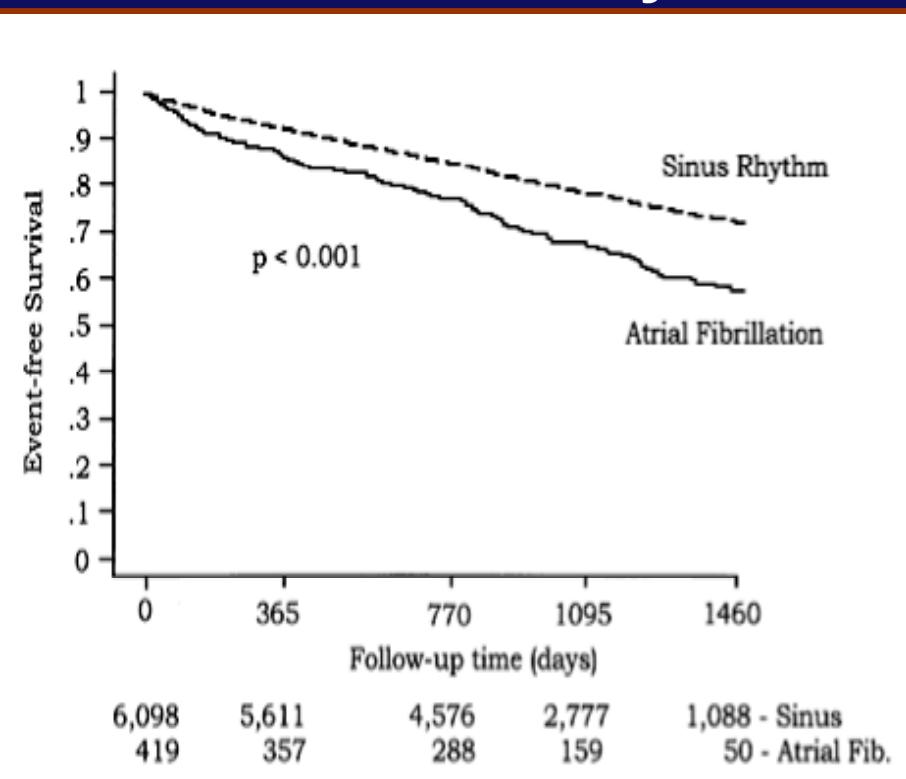
TABLE 2. Cox Multivariable Proportional Hazards Models Examining the Impact of the Comorbid Condition on Mortality

Models	Men, Adjusted HR (95% CI)	Women, Adjusted HR (95% CI)
Comorbid condition as a time-dependent variable		
(A) Mortality after AF		
Impact of incident CHF	2.7 (1.9 to 3.7)*	3.1 (2.2 to 4.2)*
(B) Mortality after CHF		
Impact of incident AF	1.6 (1.2 to 2.1)†	2.7 (2.0 to 3.6)*
Comorbid condition as a categorical variable		
(C) Mortality after AF		
Impact of prior CHF	2.2 (1.6 to 3.0)*	1.8 (1.3 to 2.3)*
Impact of concurrent CHF‡	2.4 (1.6 to 3.5)*	1.4 (1.0 to 1.9)
(D) Mortality after CHF		
Impact of prior AF	0.8 (0.6 to 1.0)	1.2 (0.9 to 1.6)
Impact of concurrent AF‡	1.0 (0.7 to 1.4)	1.1 (0.8 to 1.5)

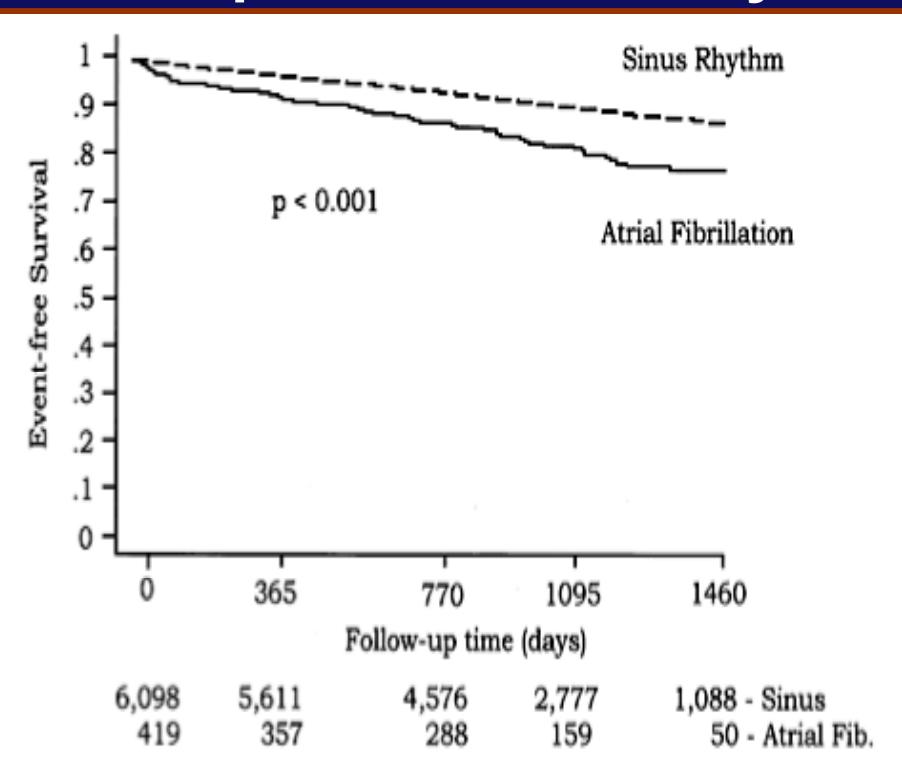
From Wang et al, NEJM 2003

AF vs NSR in Heart Failure: SOLVD

Total Mortality



Pump Failure Mortality

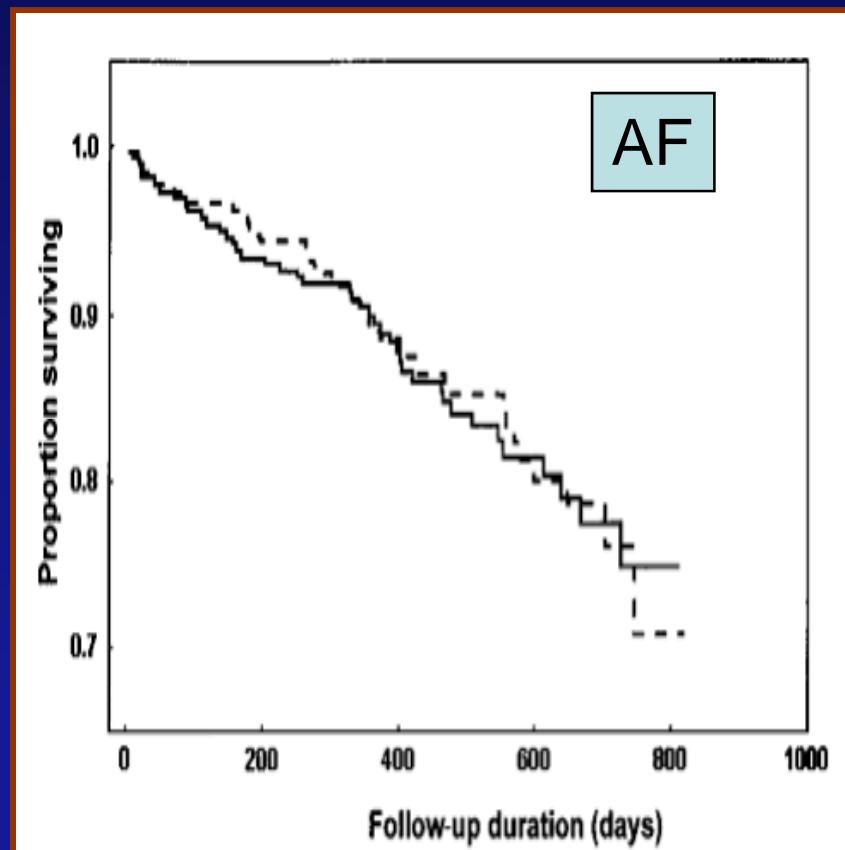
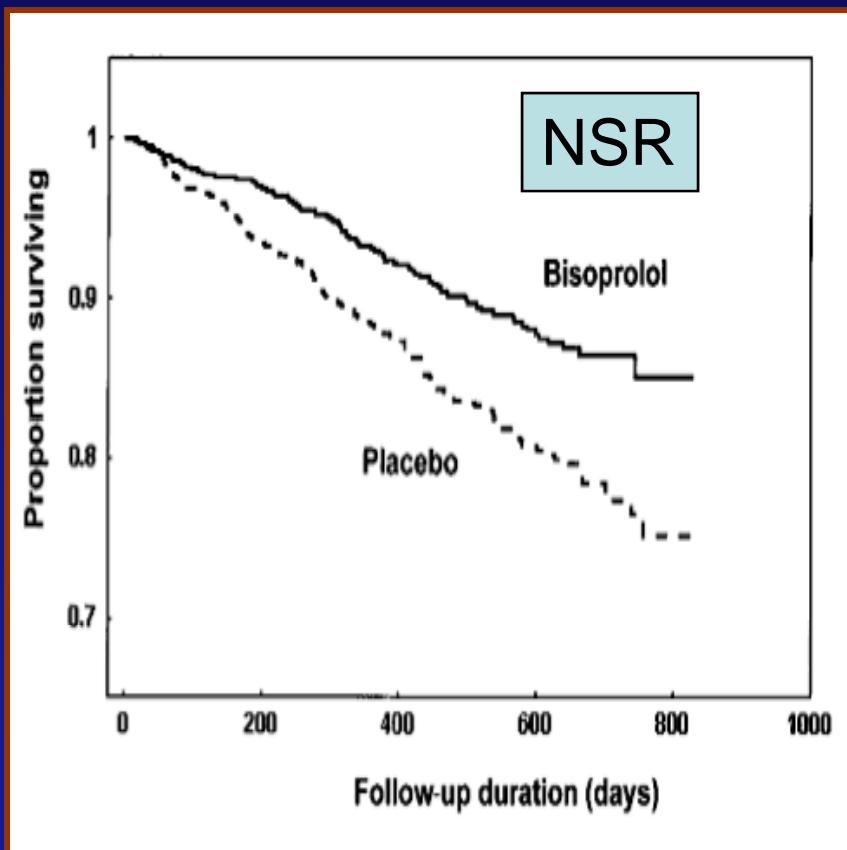


Dries et al, JACC 1998

Possible Reasons for Adverse Effect of AF on Prognosis With HF

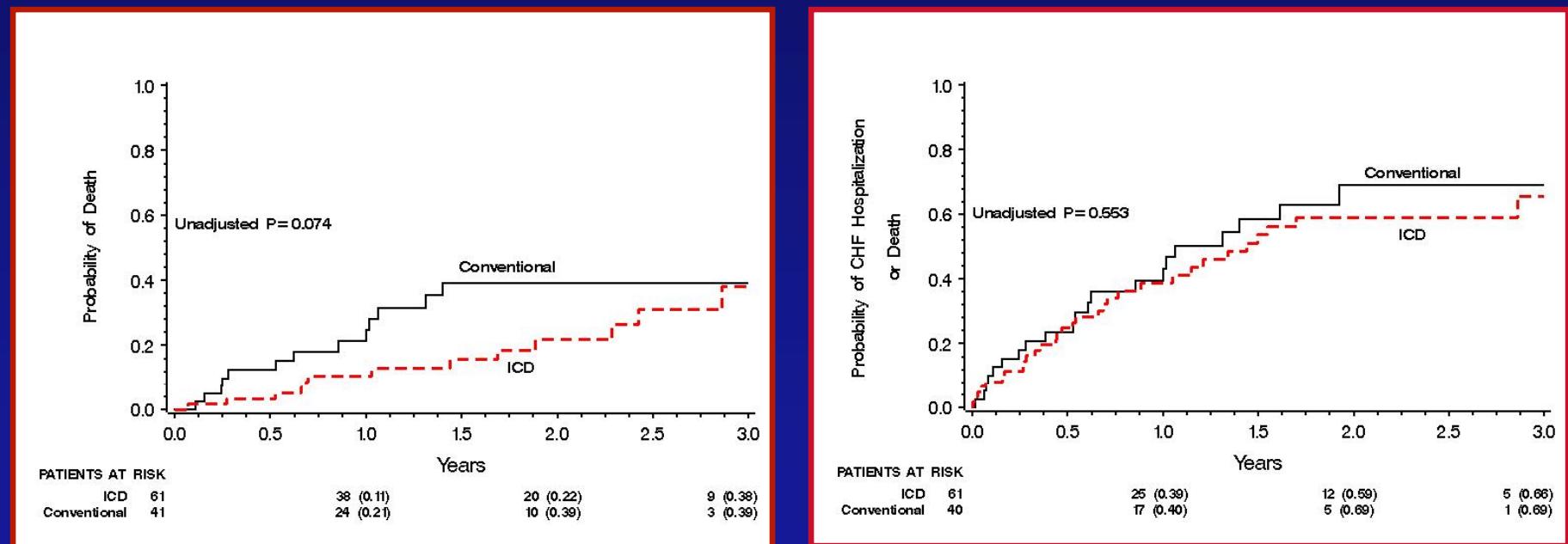
- Rapid and nonphysiologic ventricular rate
 - Diminished ventricular filling
 - Tachycardia-related cardiomyopathy
 - Pure/impure
 - Myocardial ischemia
 - Increased O₂ demand
 - Decreased coronary perfusion
 - Rate-related ventricular conduction delay
- Abnormal neurohormonal response
- Irregularly irregular pattern
 - Aggravation ventricular dysfunction and hemodynamic abnormalities
 - Increased ventricular electrical instability and VT/VF risk
- Loss of atrial kick
 - Decreased stroke volume
- Hypercoagulable state
 - Increased stroke risk
 - Possible increased thrombotic potential in other vascular territories

Failure of Beta Blocker Benefit



From Lechat et al, Circulation 2001

ICD Value in High Risk AF: Results from MADIT II

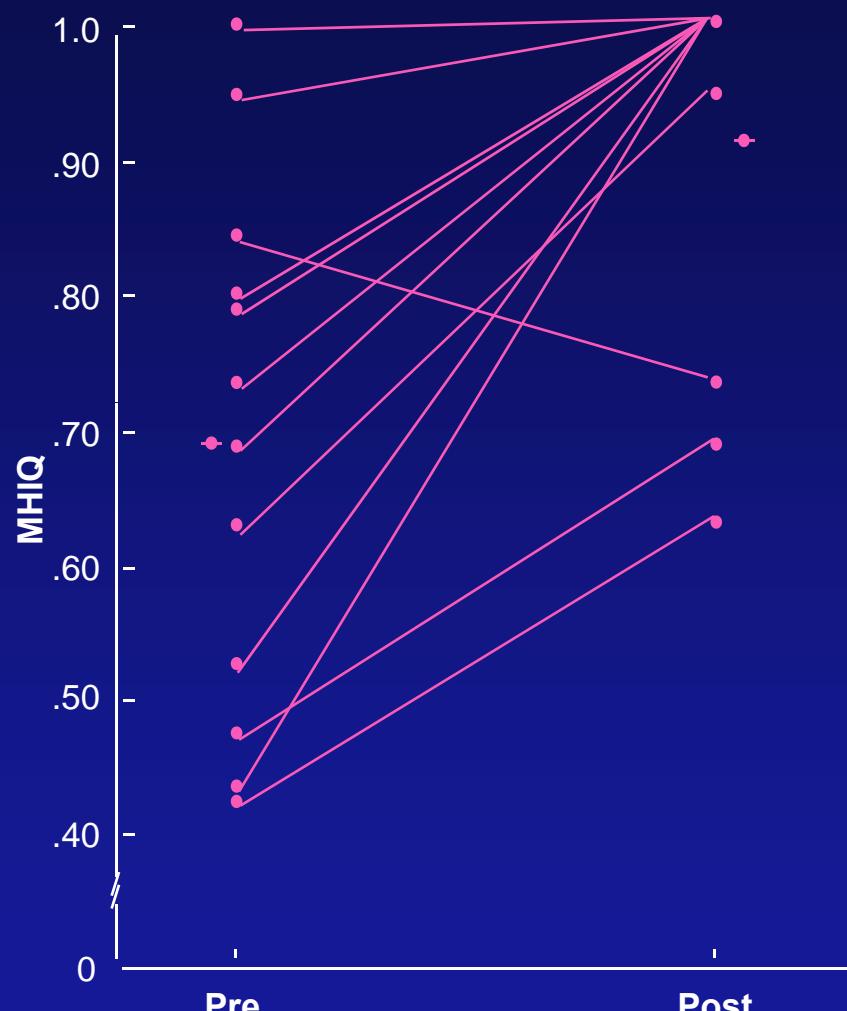


Zareba et al, AJC 2006

Therapeutic Objectives

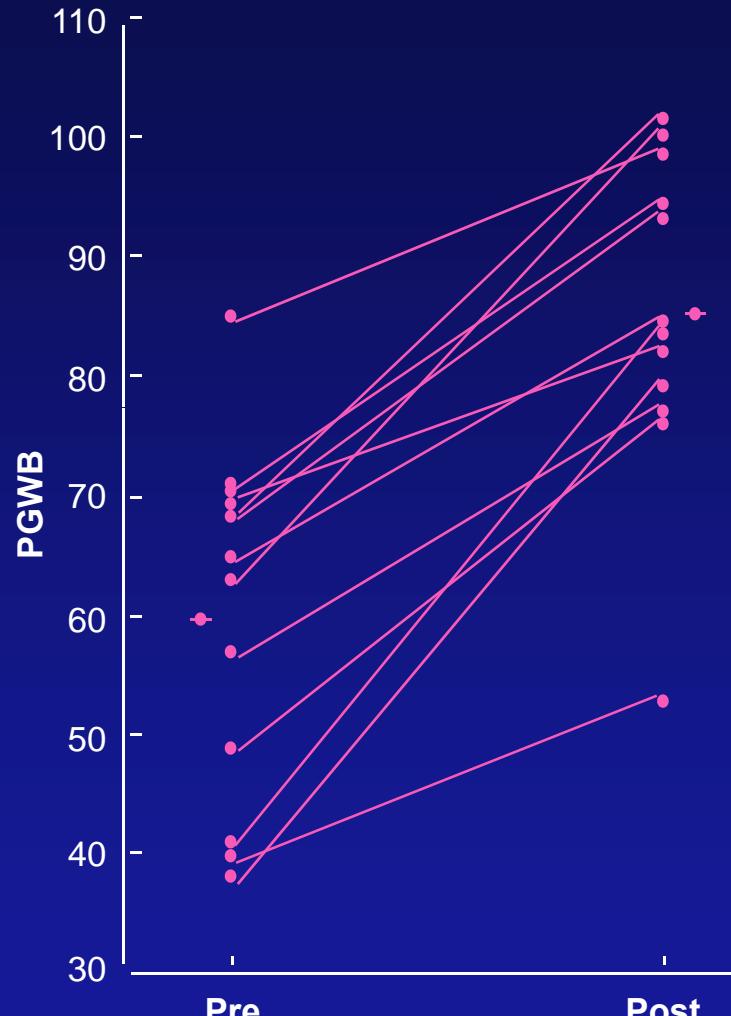
- Symptom relief
- Stroke prevention
- Rhythm control
- Rate control
 - Medical therapy with AVN blockers
 - AVJ ablation and pacemaker (“Ablate + Pace”)

Subjective Benefits of Ablate + Pace



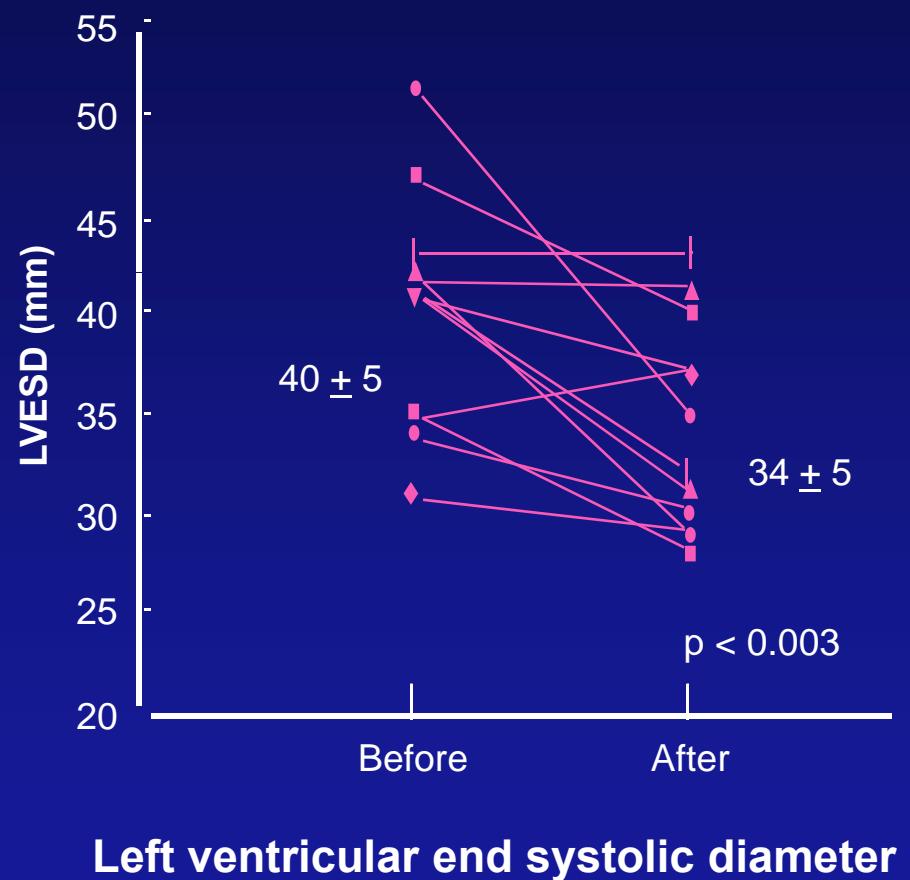
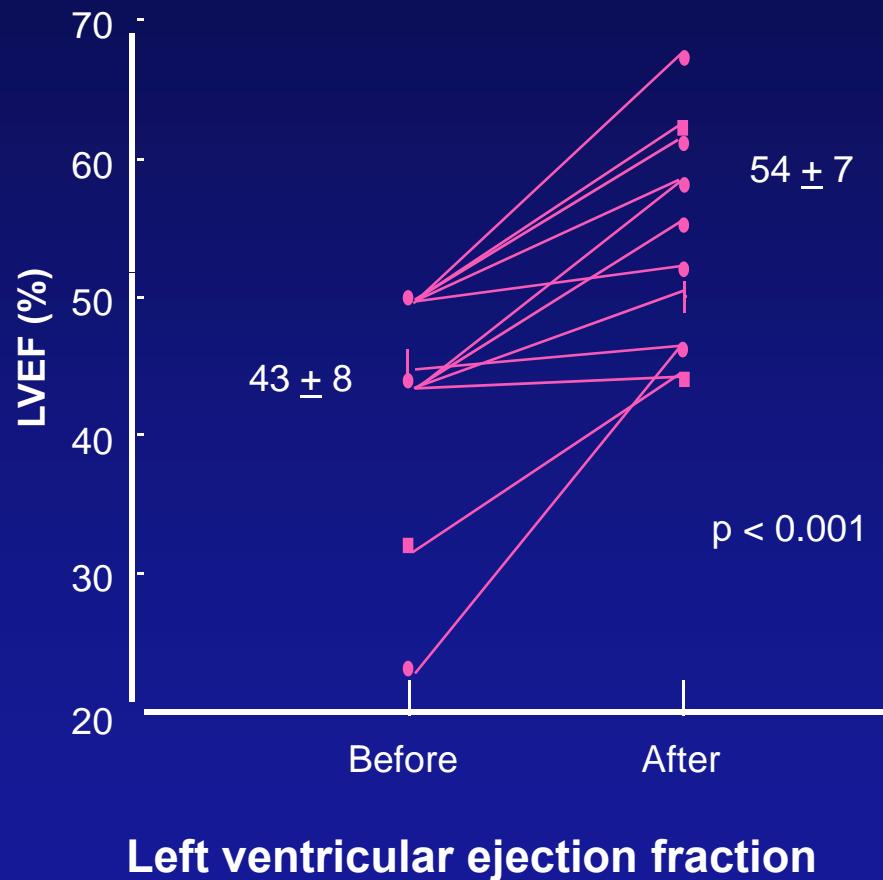
McMaster Health Index Questionnaire

Kay et al, AJC 1988



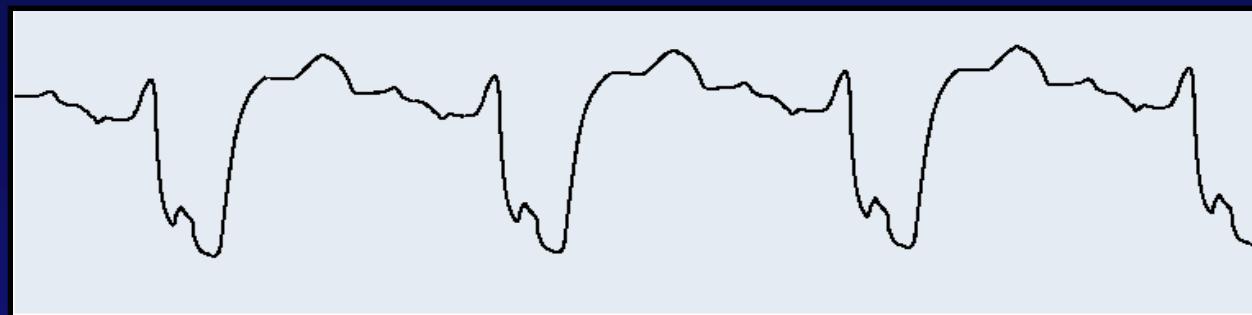
Psychological General Well-Being Index

Objective Benefits of Ablate + Pace



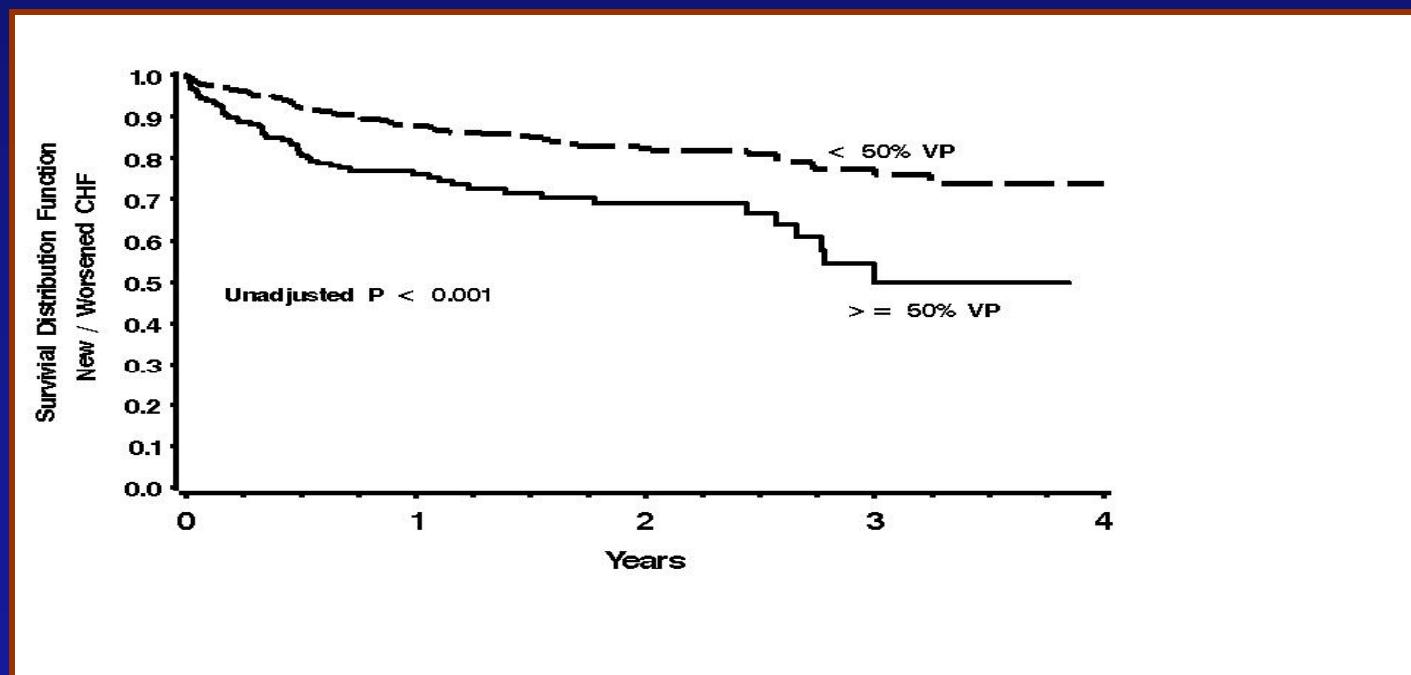
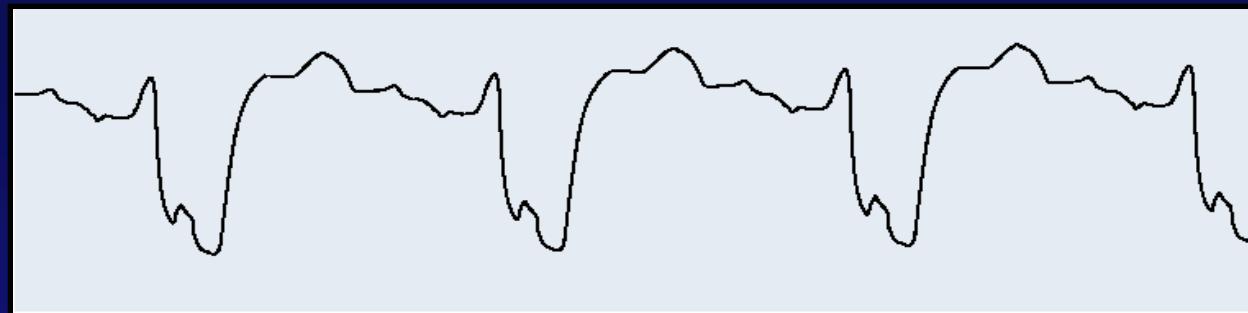
Rodriguez et al, AJC 1993

Problem With Chronic RV Pacing



Steinberg et al, JCE 2005

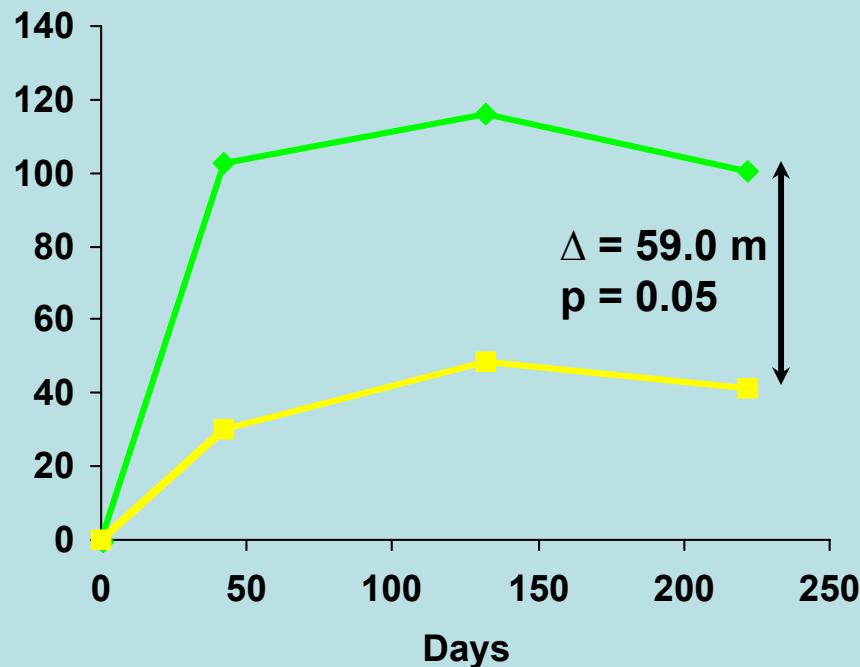
Problem With Chronic RV Pacing



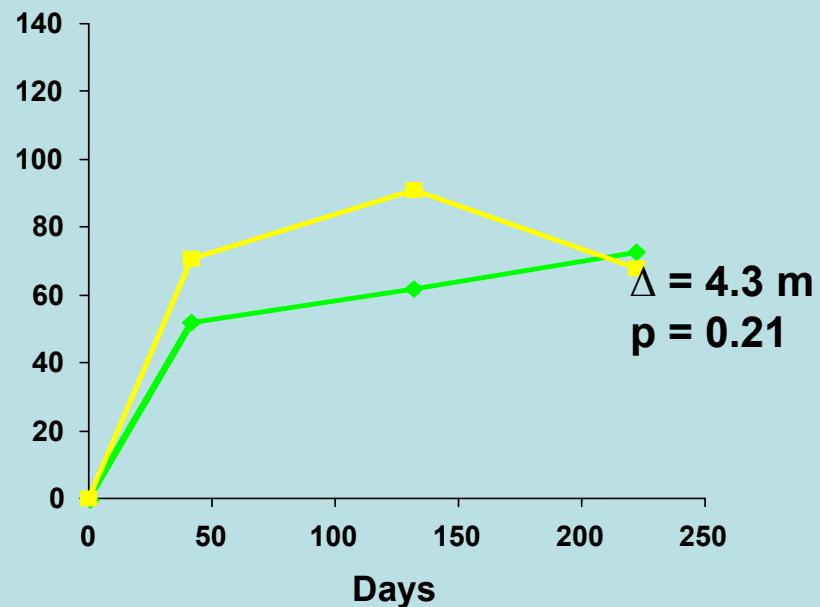
Steinberg et al, JCE 2005

PAVE: Results of 6-Minute Walk Relative to LVEF

LVEF \leq 35%



LVEF > 35%



█ BV (N = 23)
█ RV (N = 26)

█ BV (N = 68)
█ RV (N = 48)

CRT in Heart Failure and AF: MUSTIC - AF

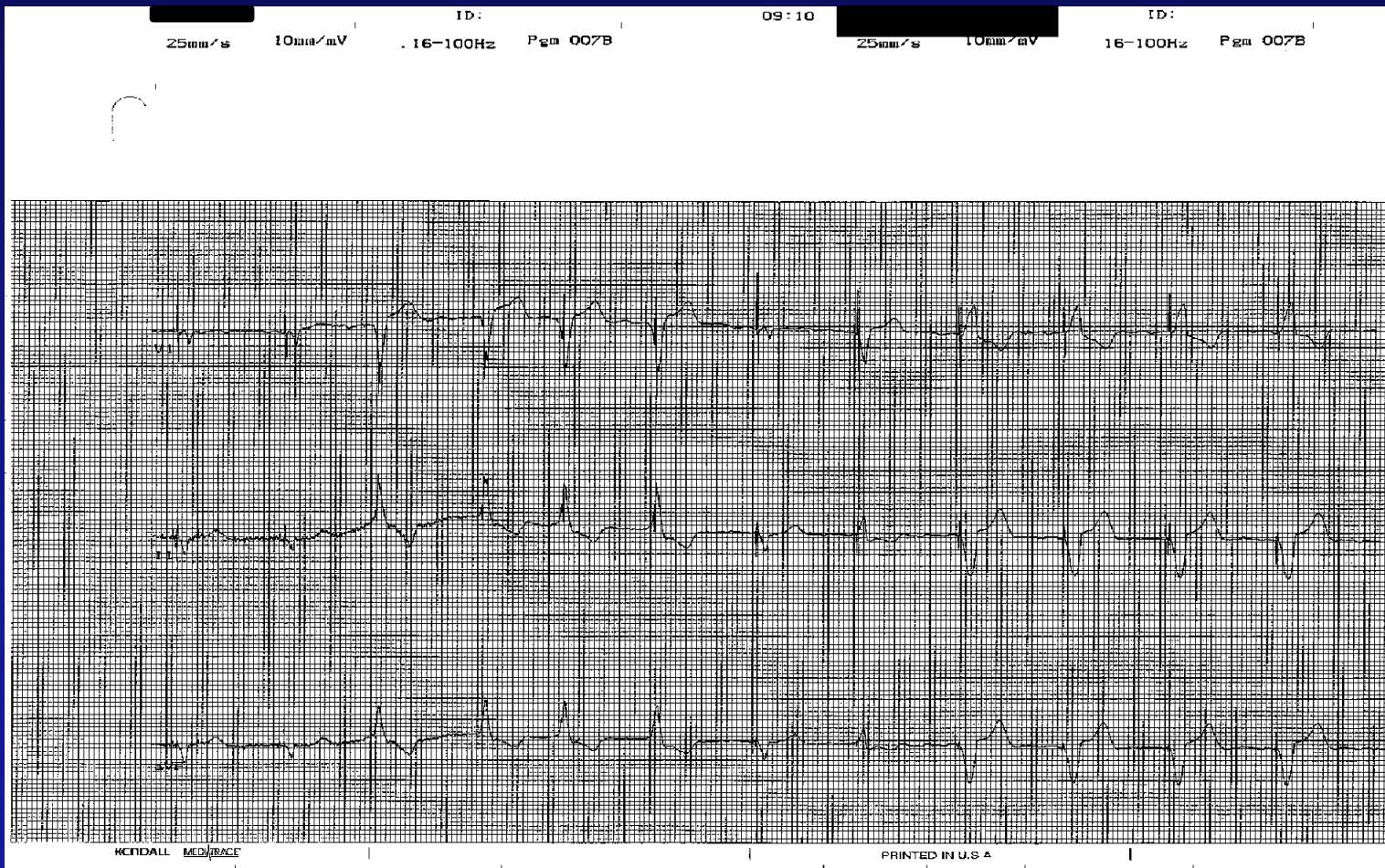
- N = 59
- Class III HF, LVEF < 35%
- Chronic AF and “slow” ventricular rate
- 6 month randomized crossover design: RVP vs BVP; 1o endpoint = 6 min walk
- Only 39 pts completed study
- No difference in 6 min walk: 341m vs 359m, respectively, and no difference in QoL
- More pts preferred BVP

Challenges to Achieving Consistent BV Capture in Patients With AF

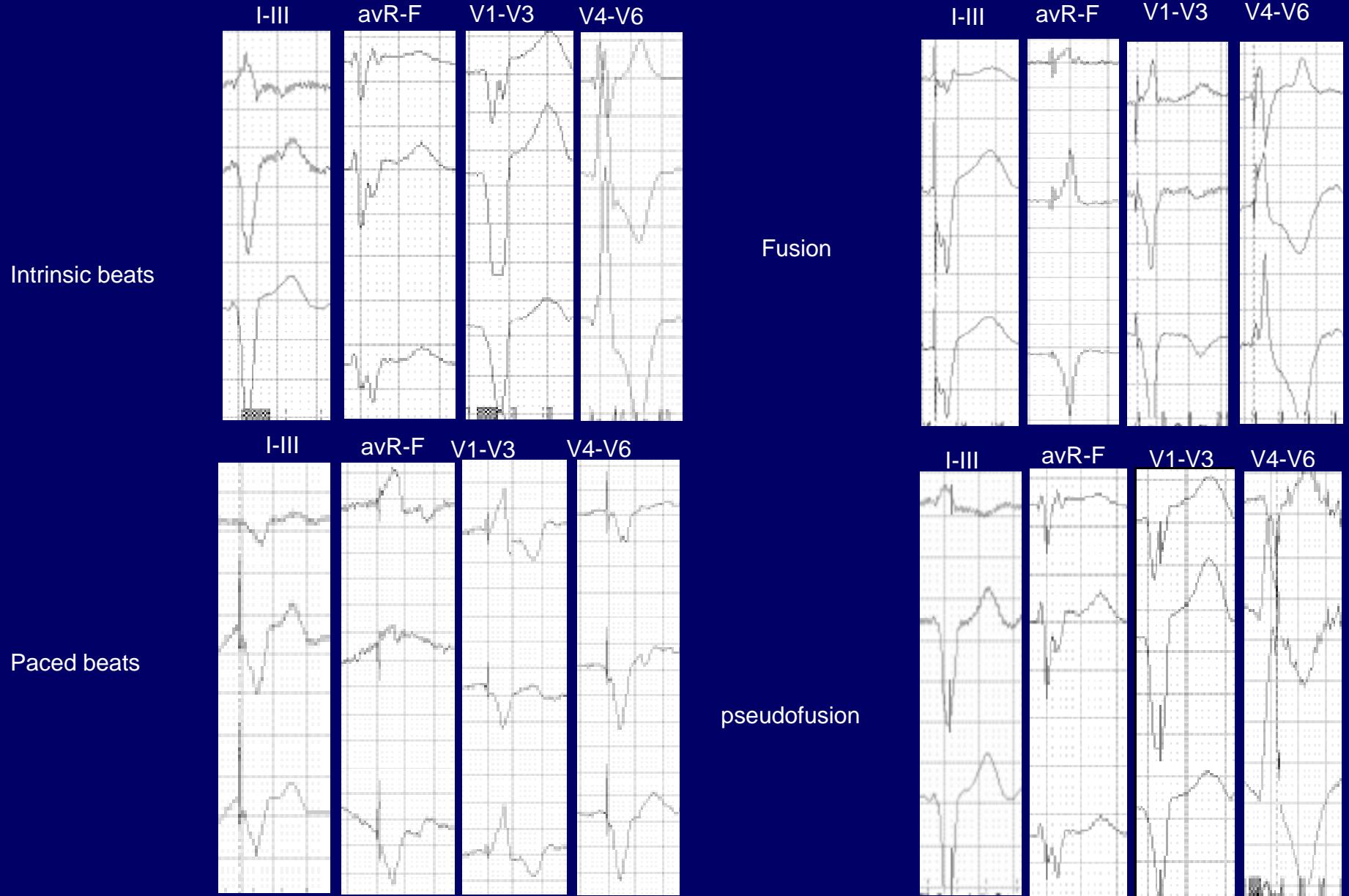
- Higher intrinsic heart rate necessitates higher programmed pacing rate
- Frequent fusion beats
- Frequent pseudofusion beats
- Inaccurate assessment of BV capture by device counters

Steinberg, JACC 2006

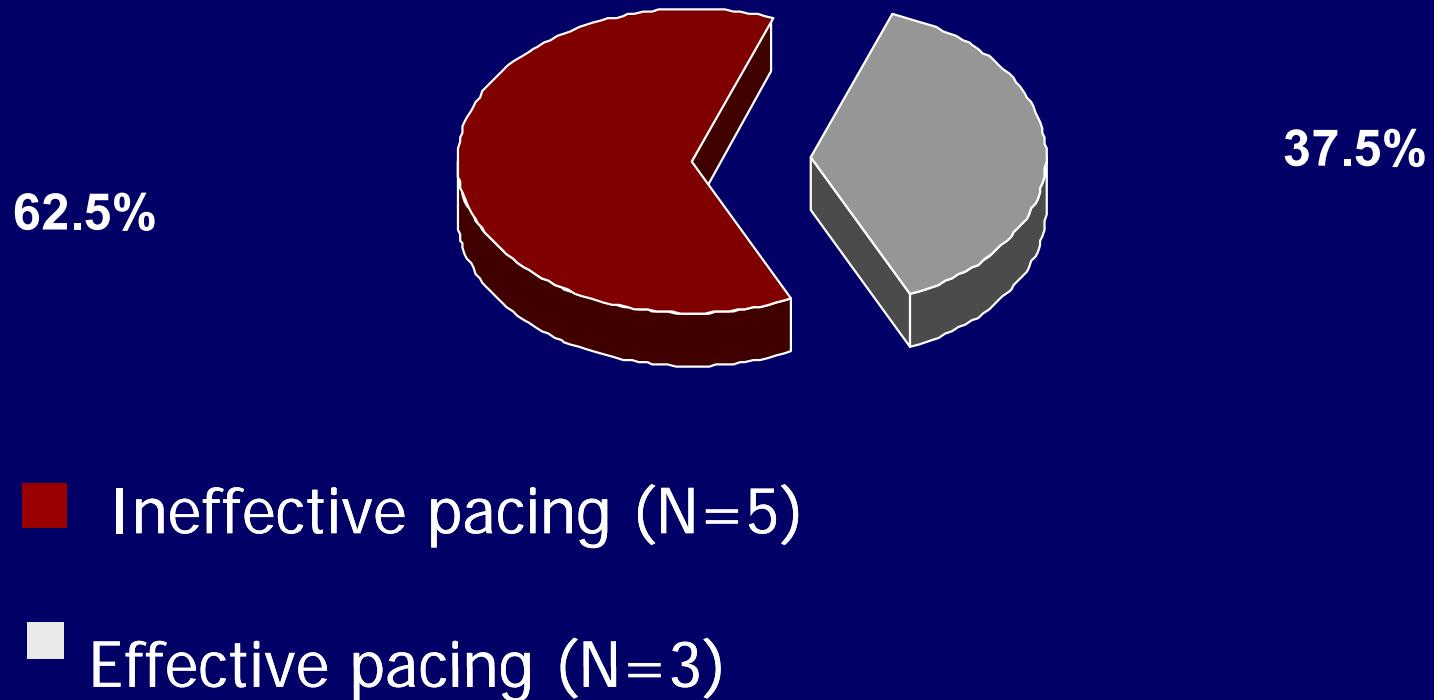
Example of Problematic BV Pacing



Definition of Pacing Complexes

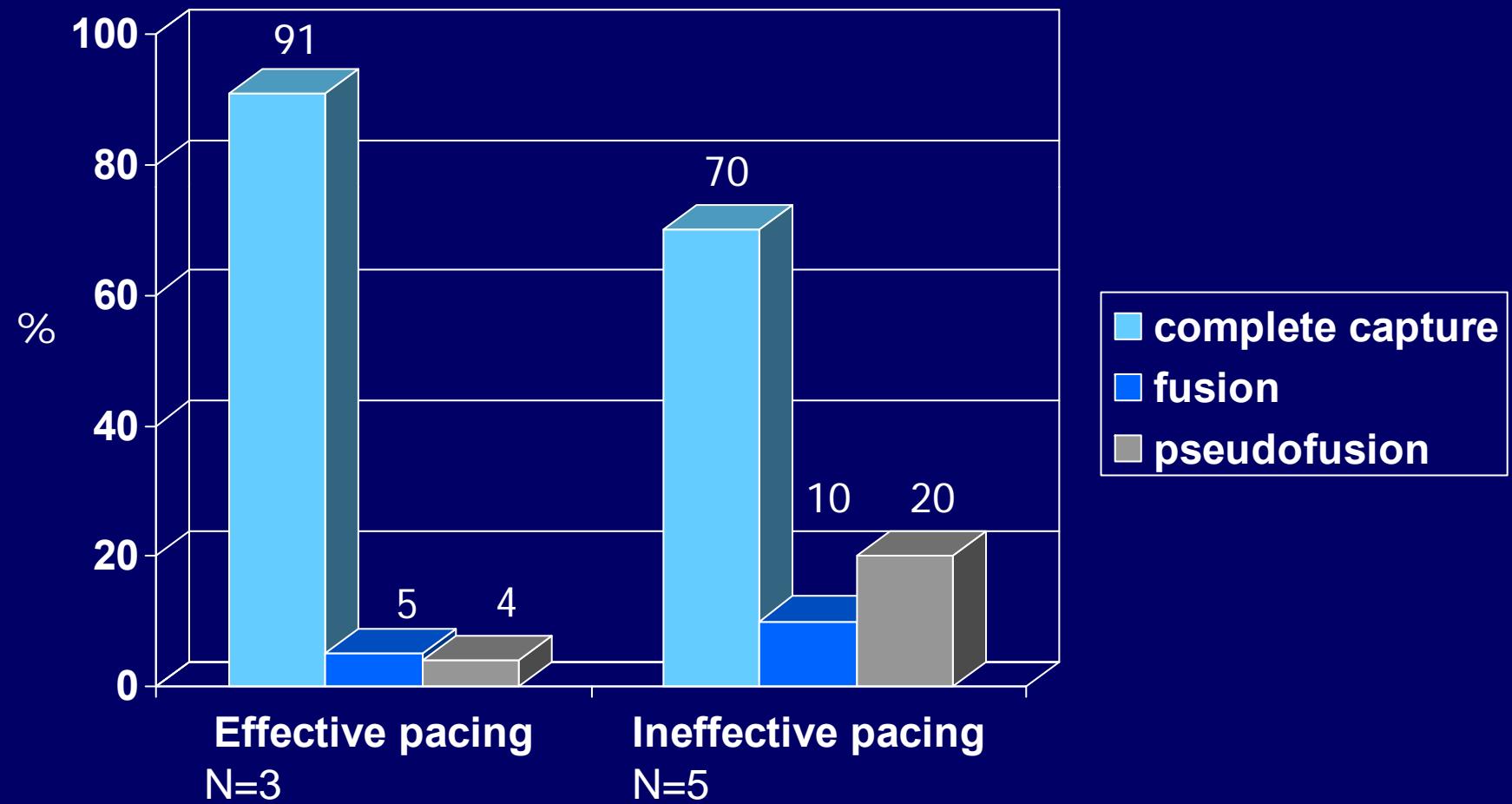


Proportion of Effective vs. Ineffective Pacing



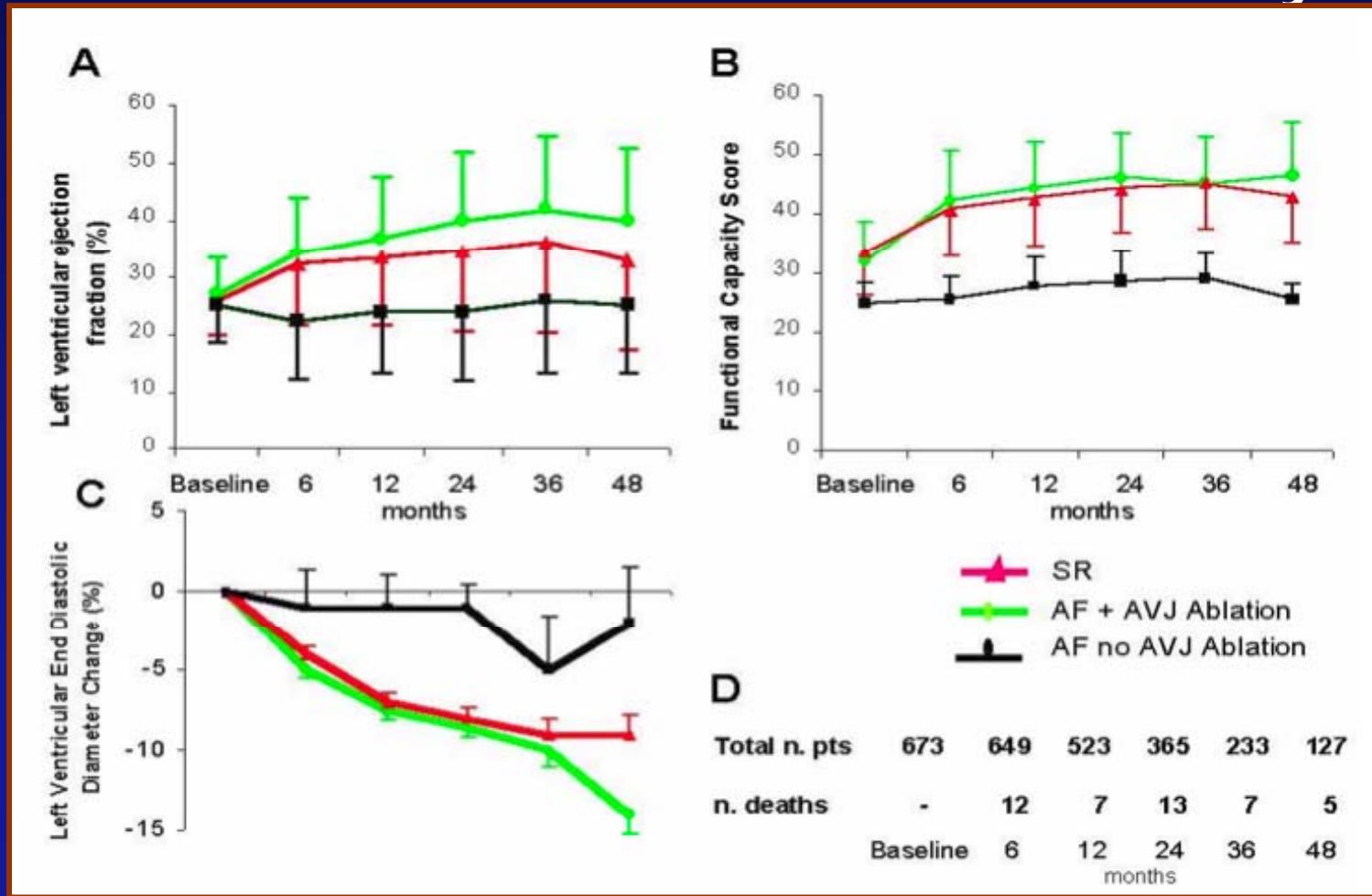
Cotiga et al, Circulation 2006

Holter Data



Cotiga et al, Circulation 2006

CRT Employed in AF: Outcomes From Observational Study

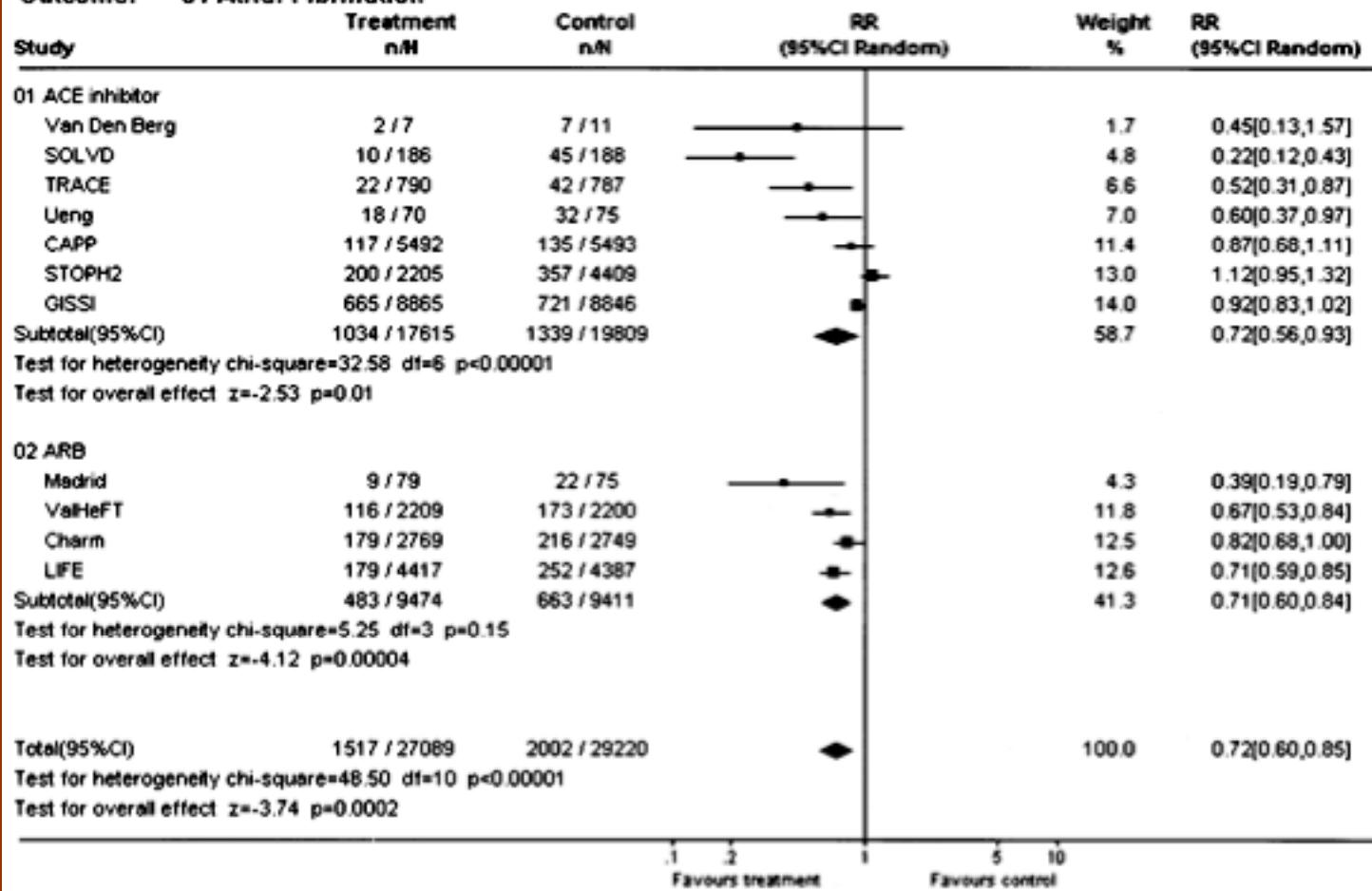


Courtesy of Gasparini et al

Inhibition of the R-A-A-S

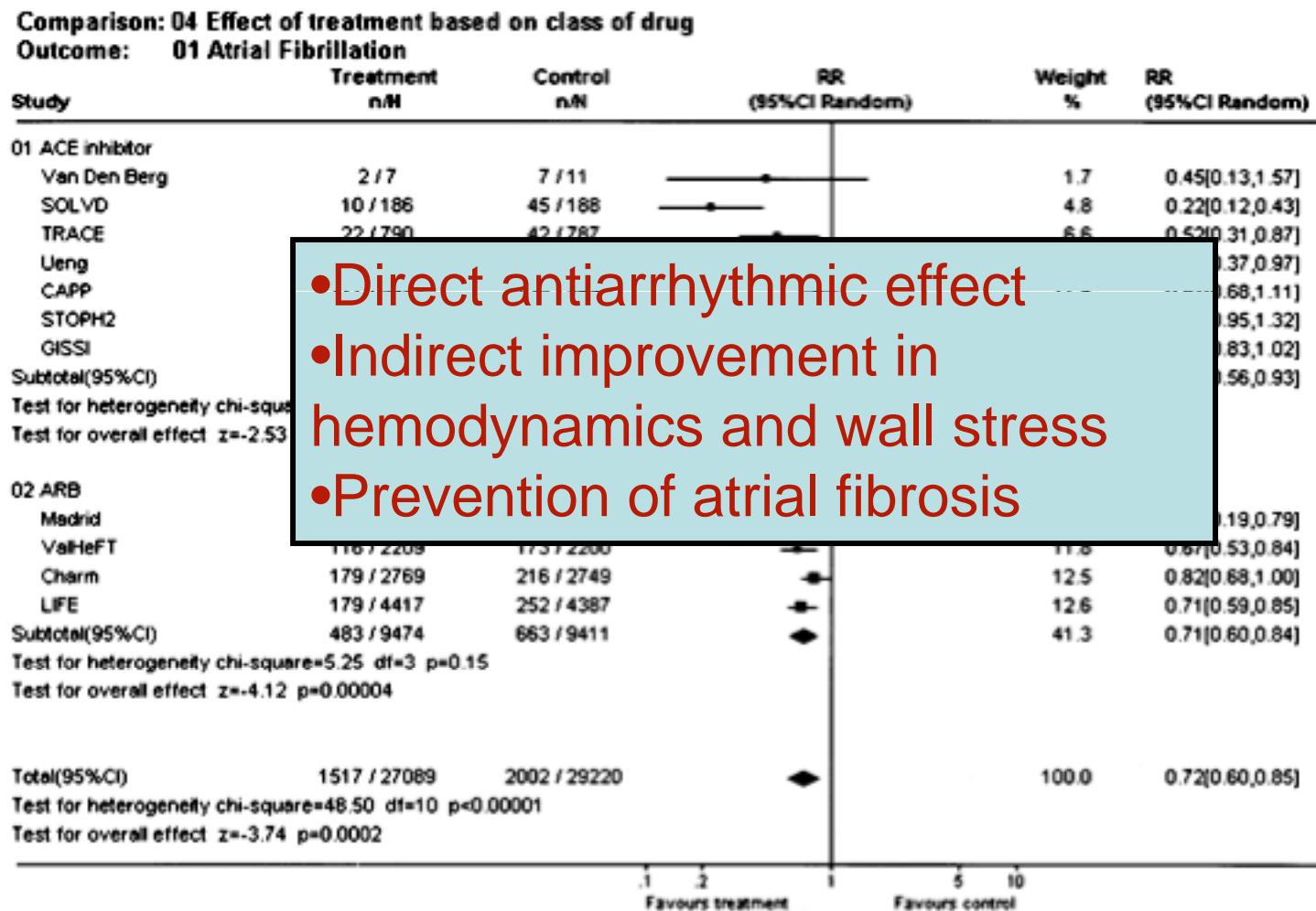
Comparison: 04 Effect of treatment based on class of drug

Outcome: 01 Atrial Fibrillation



From Healy et al, JACC 2005

Inhibition of the R-A-A-S



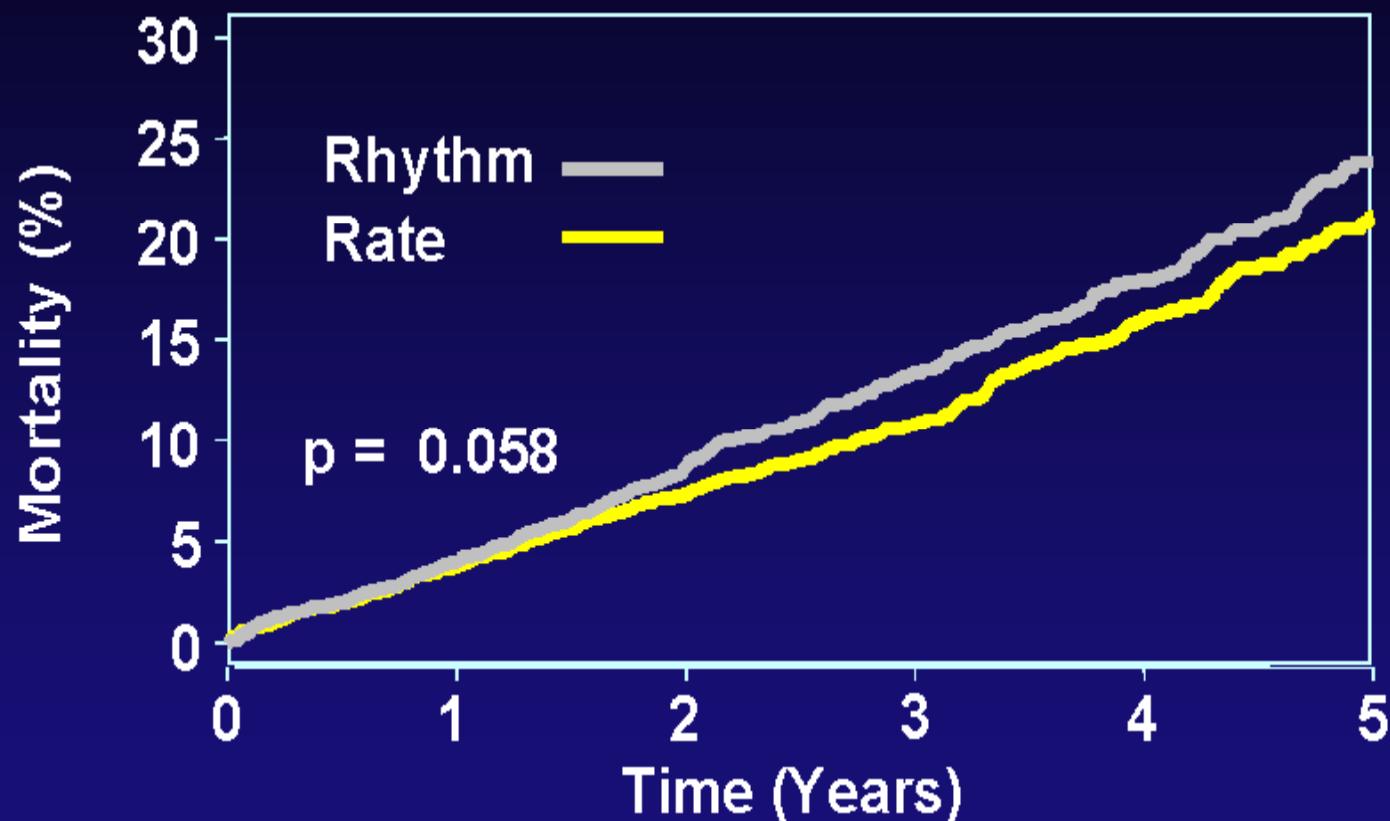
From Healy et al, JACC 2005

Rhythm Control Strategy

- DIAMOND-CHF
 - Substudy - 506 pts with EF<0.35 in atrial flutter or AF at baseline showed that sinus rhythm at 1 yr was associated with improved survival whether on dofetilide or placebo
- CHF-Stat
 - Conversion to sinus rhythm on amiodarone led to improved survival



Primary Endpoint: All-Cause Mortality

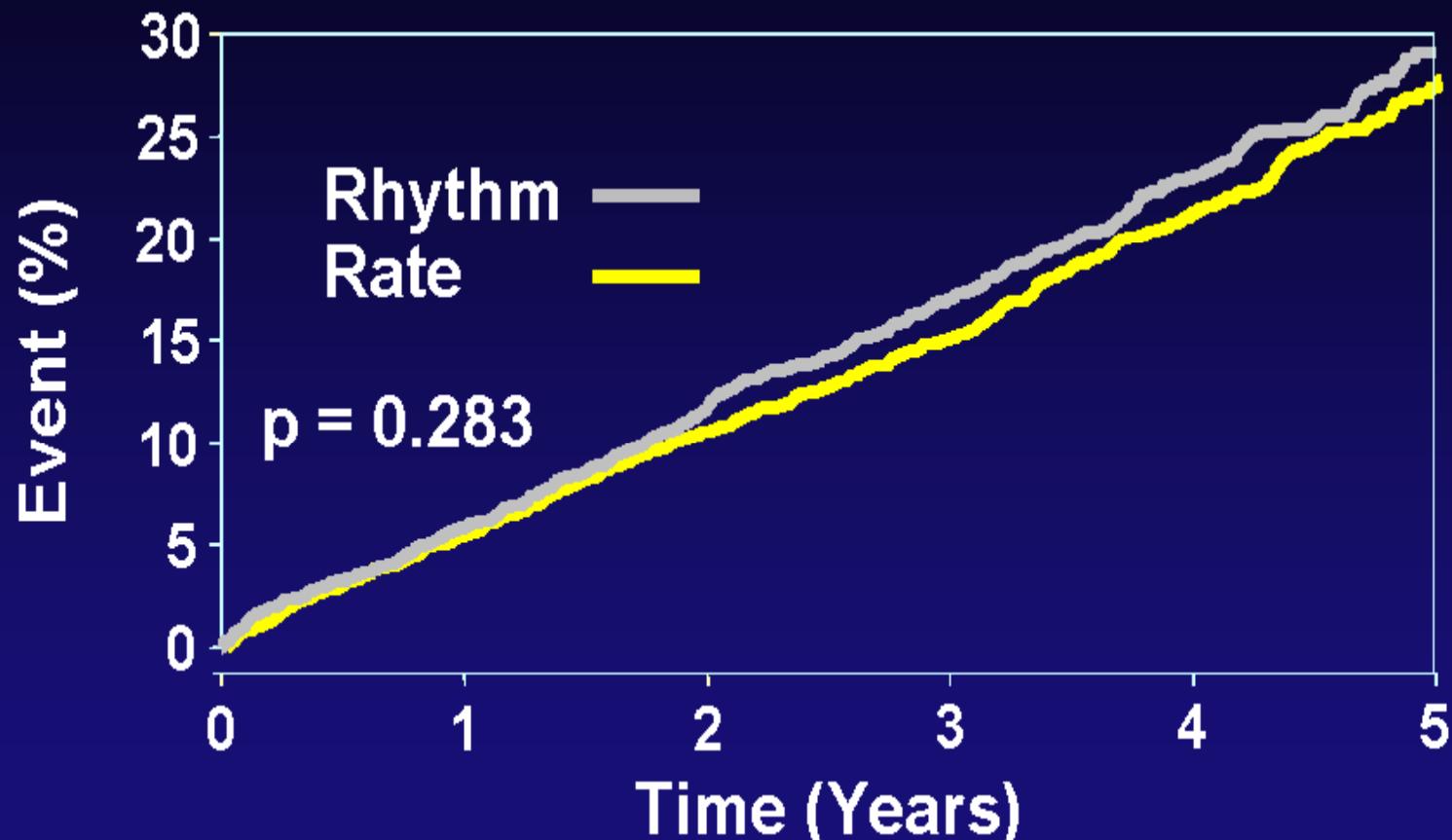


Rhythm N: 2033 1932 1807 1316 780 255

Rate N: 2027 1925 1825 1328 774 236

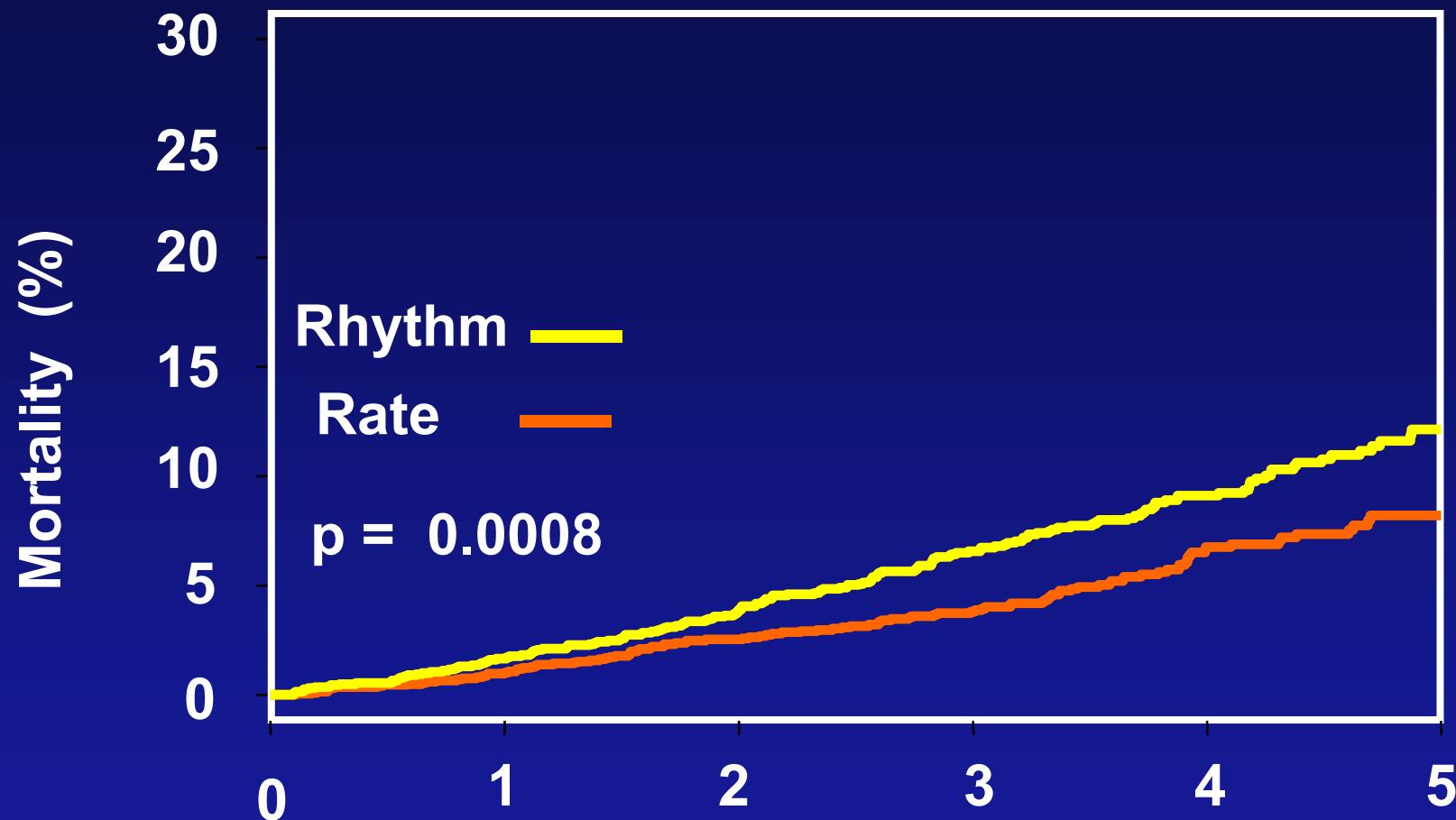


Secondary Endpoint- Death, Disabling Stroke or Anoxic Encephalopathy, Major Bleed, or Cardiac Arrest



Rhythm N:	2033	1895	1746	1259	719	231
Rate N:	2027	1889	1760	1264	722	208

AFFIRM: Non-Cardiovascular Death



Numbers of Deaths

Rhythm: 0(0%) 33(2%) 76(4%) 120(7%) 49(9%) 167(12%)

Rate: 0(0%) 20(1%) 49(3%) 70(4%) 101(7%) 109(8%)

Time (Years)

Steinberg et al, Circulation 2004

Predictors of Mortality in AFFIRM

Covariate	P-value	Hazard Ratio	99% CI
<i>Time-dependent</i>			
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
AAD use	0.0005	1.49	1.11-2.01
<i>Baseline</i>			
Age at enrollment	<0.0001	1.06	1.05-1.08
CAD	<0.0001	1.56	1.20-2.04
CHF	<0.0001	1.57	1.18-2.09
Diabetes	<0.0001	1.56	1.17-2.07
Stroke or TIA	<0.0001	1.70	1.24-2.33
Smoking	<0.0001	1.78	1.25-2.53
LV EF <50%	0.0065	1.36	1.02-1.81
Mitral valve regurgitation	0.0043	1.36	1.03-1.80

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Sinus rhythm	<0.0001	0.53	0.39-0.72
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AFFIRM Subgroup Analyses

Age < 65 (N = 969)

Age \geq 65 (N = 3091)

No CAD (N = 2509)

CAD (N = 1551)

No hypertension (N = 1184)

Hypertension (N = 2876)

No CHF (N = 3121)

CHF (N = 939)

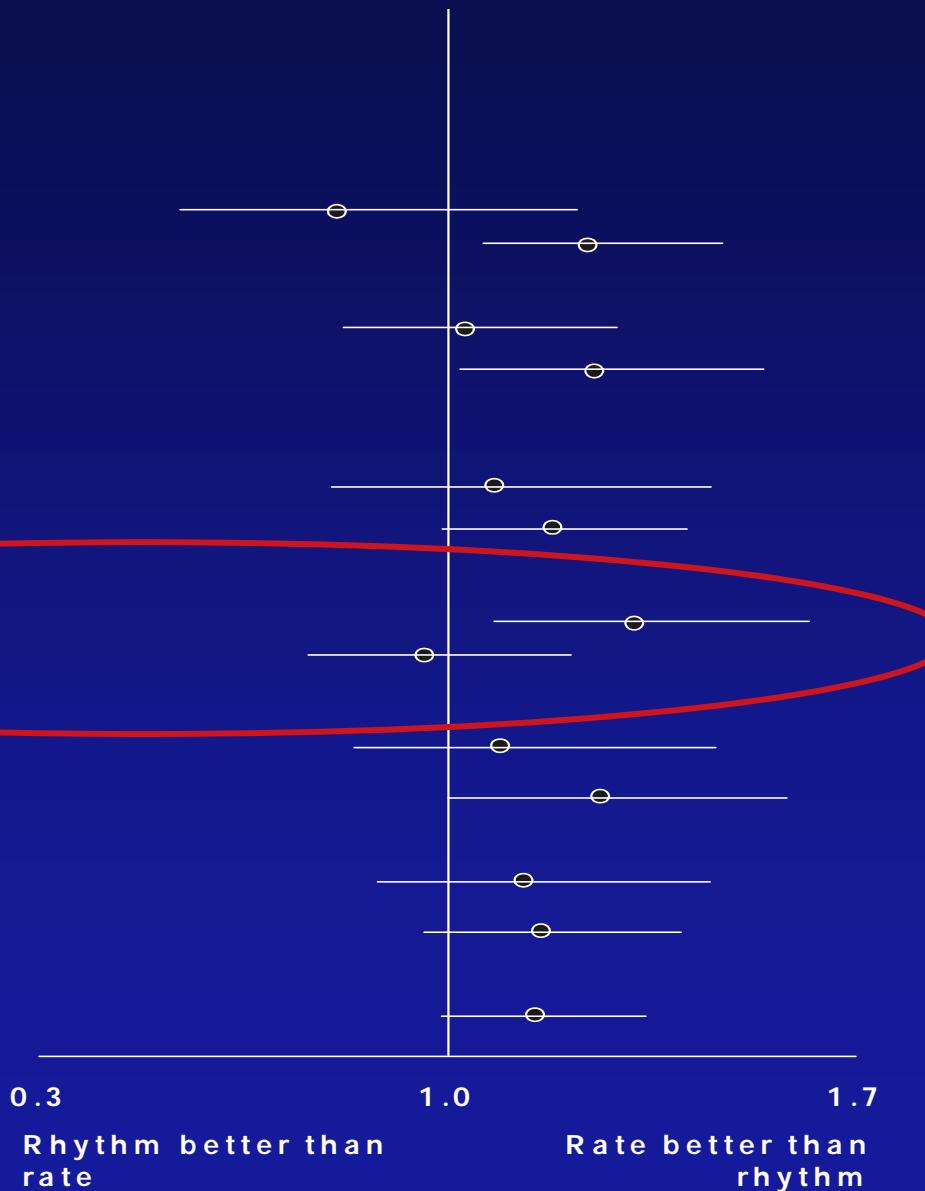
LVEF < 50% (N = 788)

LVEF \geq 50% (N = 2244)

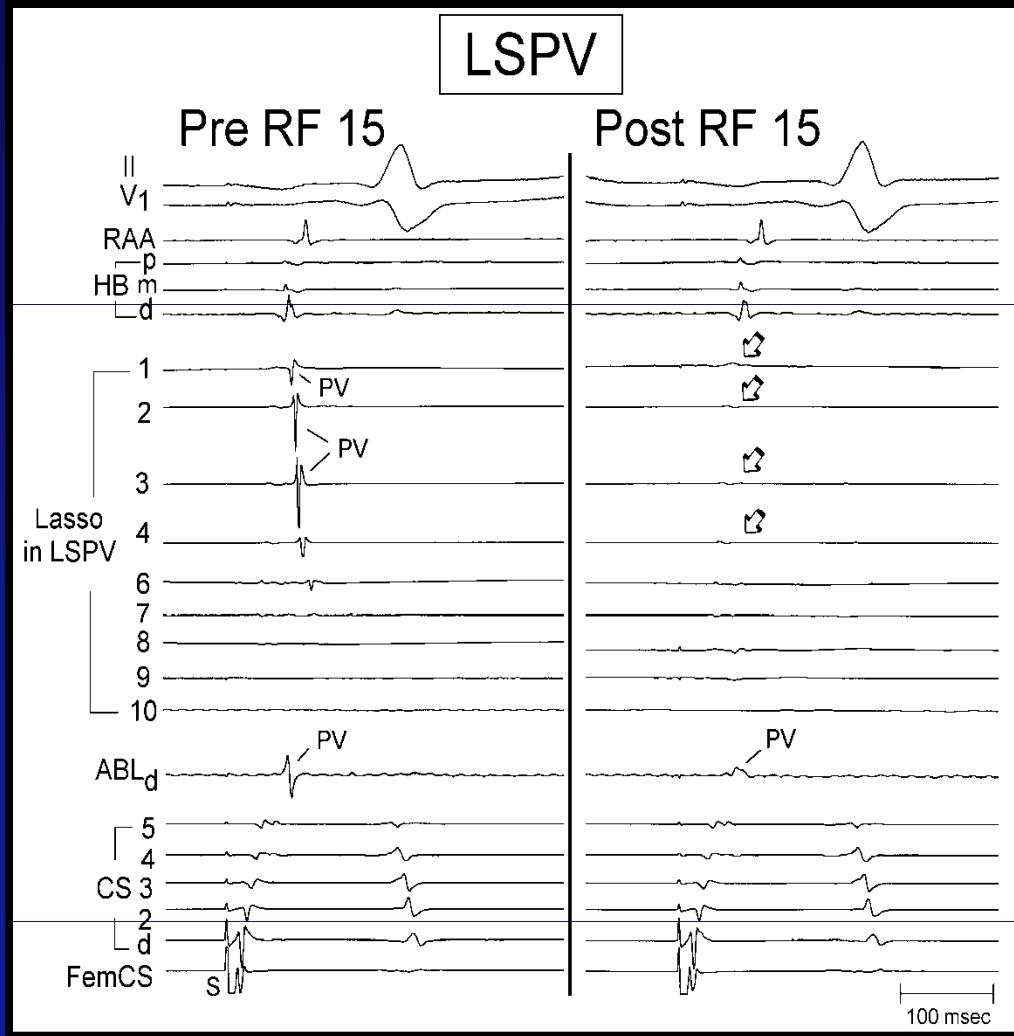
Female (N = 1594)

Male (N = 2466)

Overall (N = 4060)

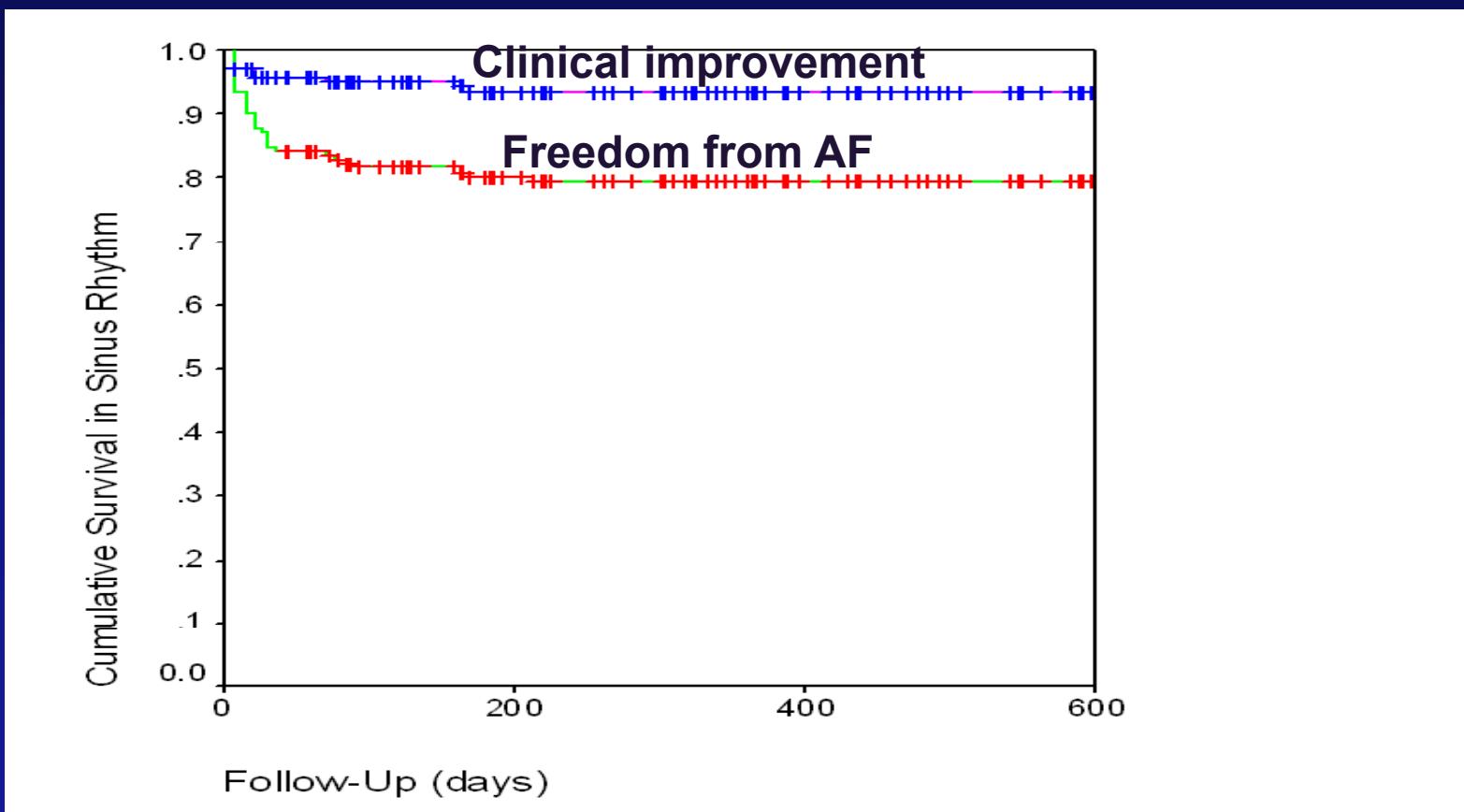


Ablation Strategy



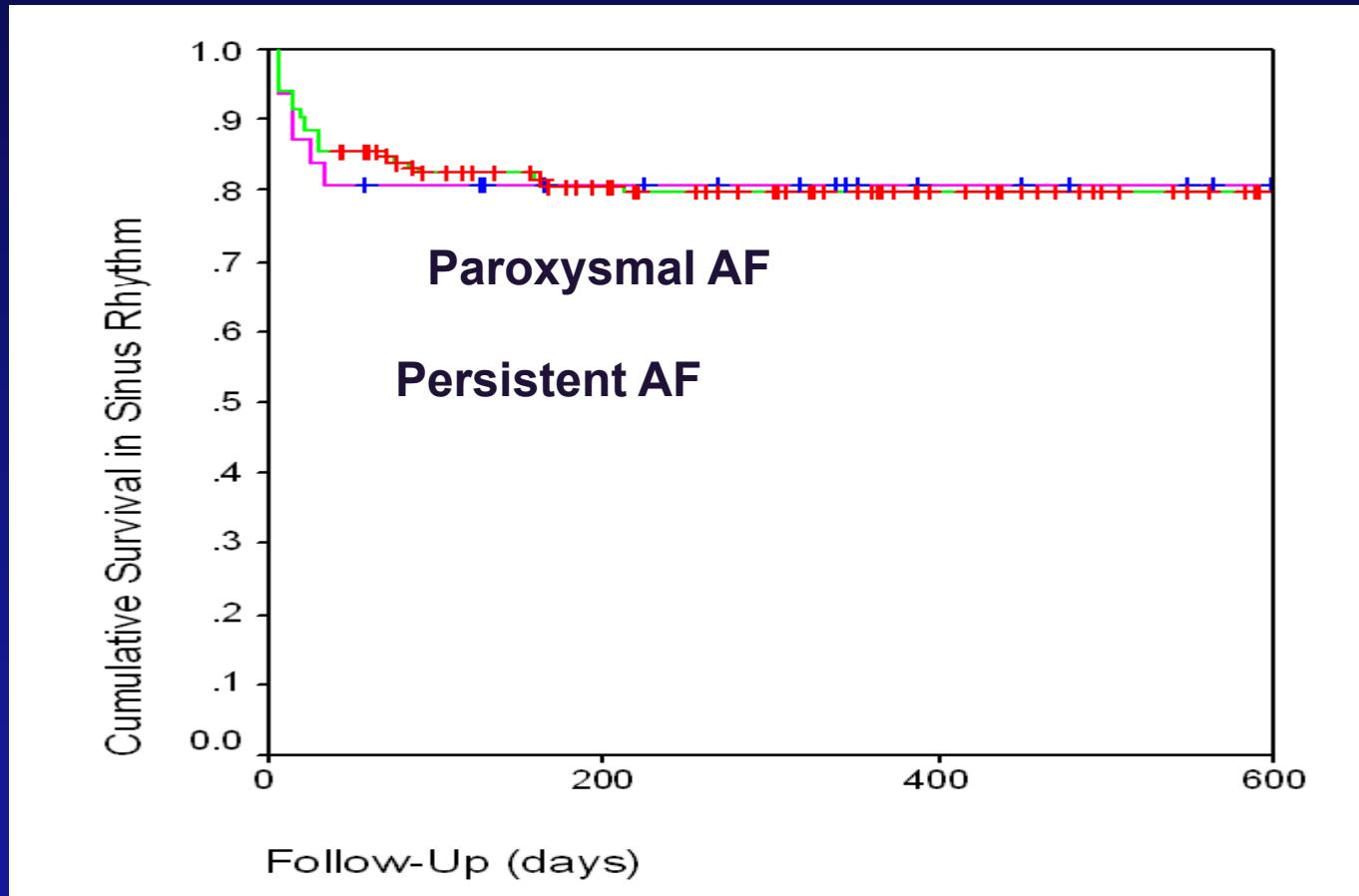
- Target the LA-PV connections at orifice
- Aim to completely isolate each and every PV
- Technically feasible in all patients

Longitudinal Follow-Up After Ablation



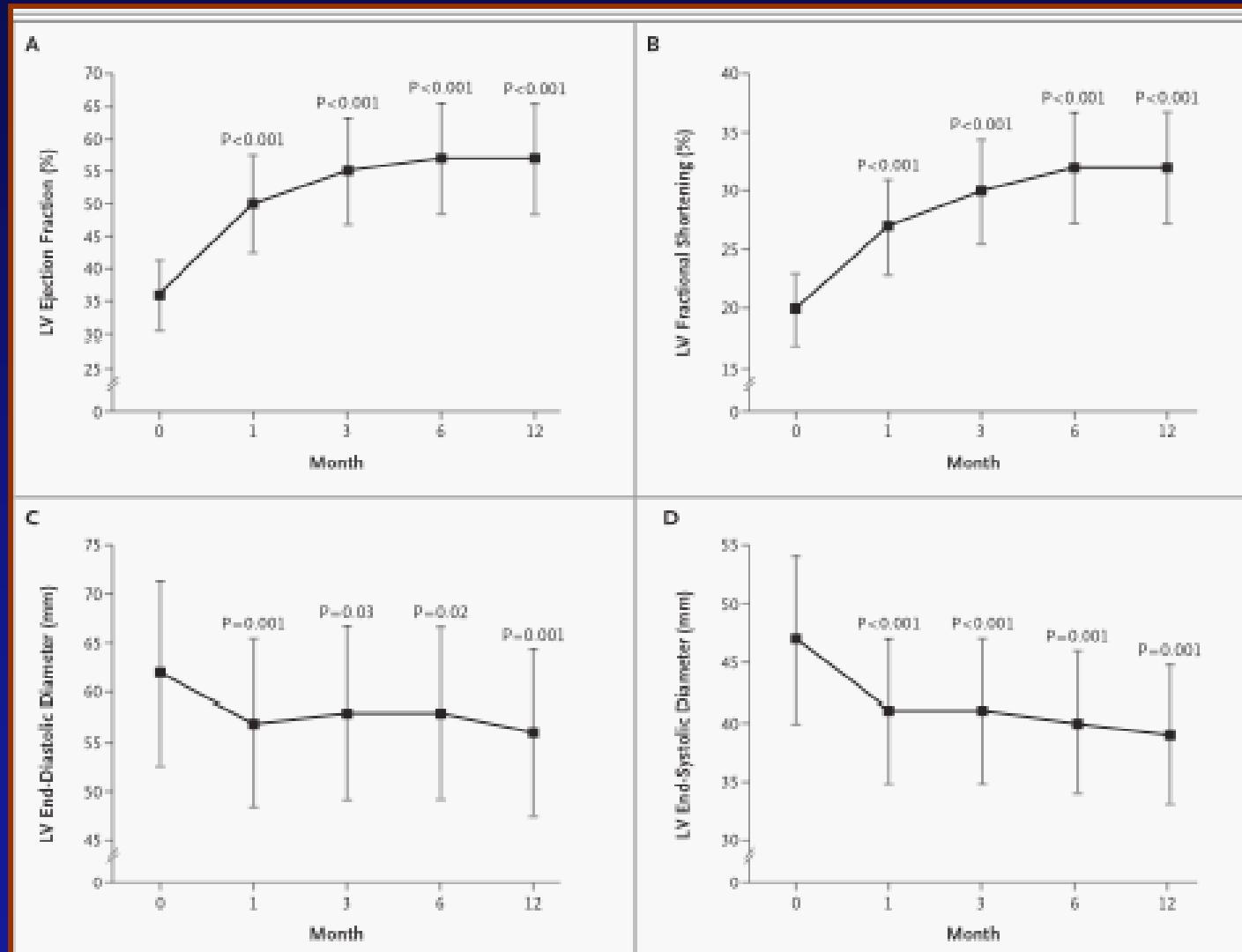
Herweg et al, AJC 2005

Outcome Relative to Type of AF



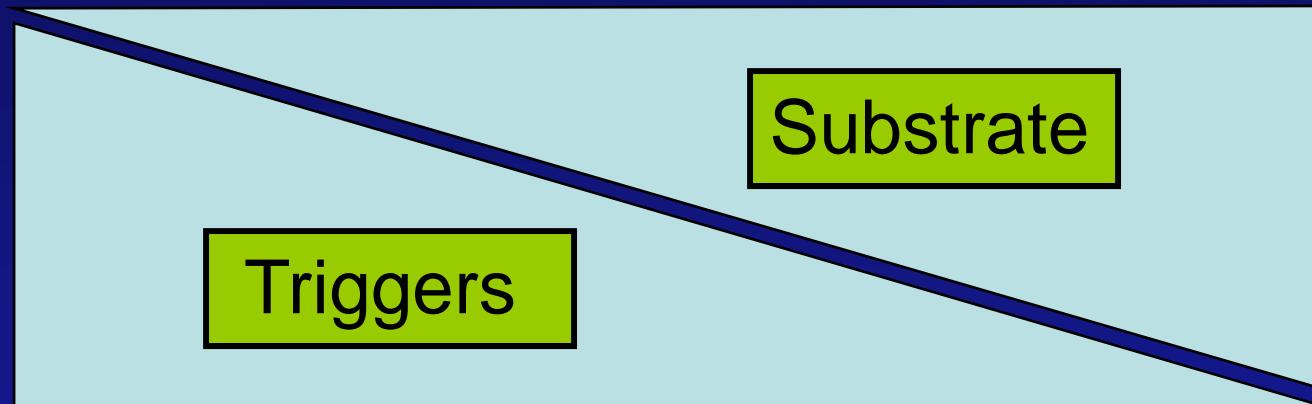
Herweg et al, AJC 2005

Ablation Outcomes in Heart Failure

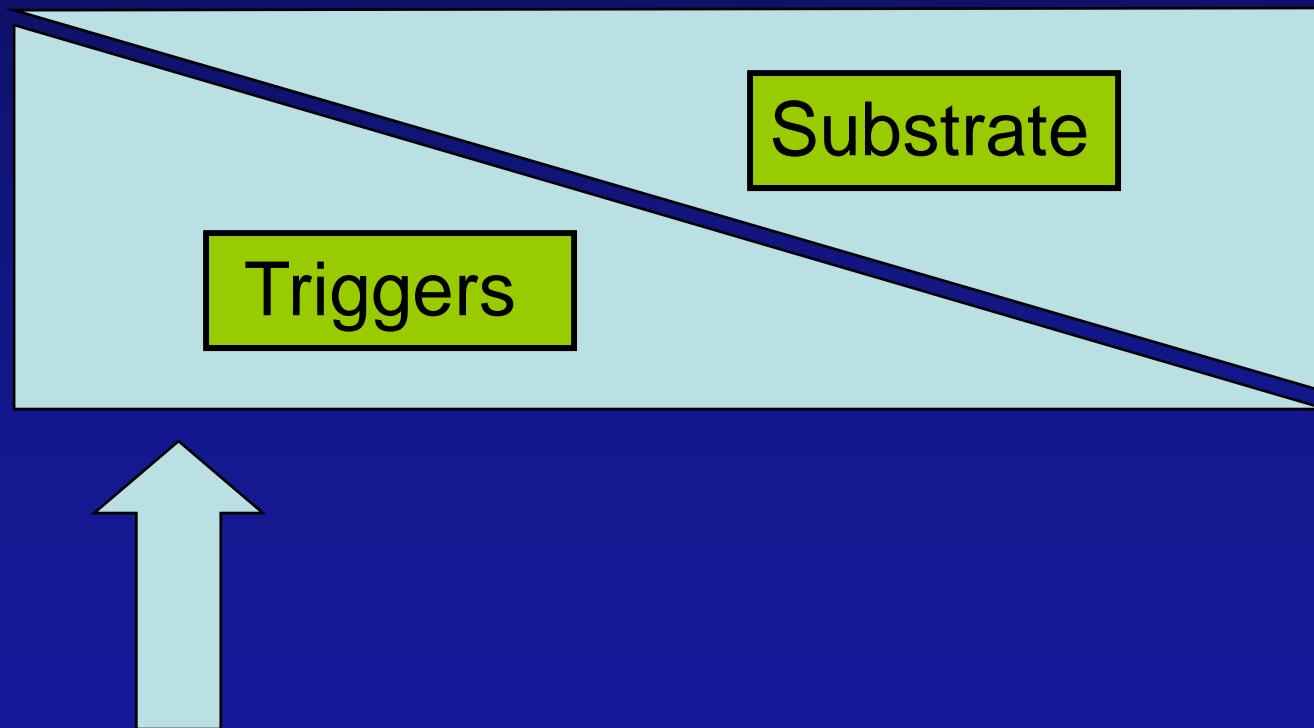


From Hsu et al, NEJM 2004

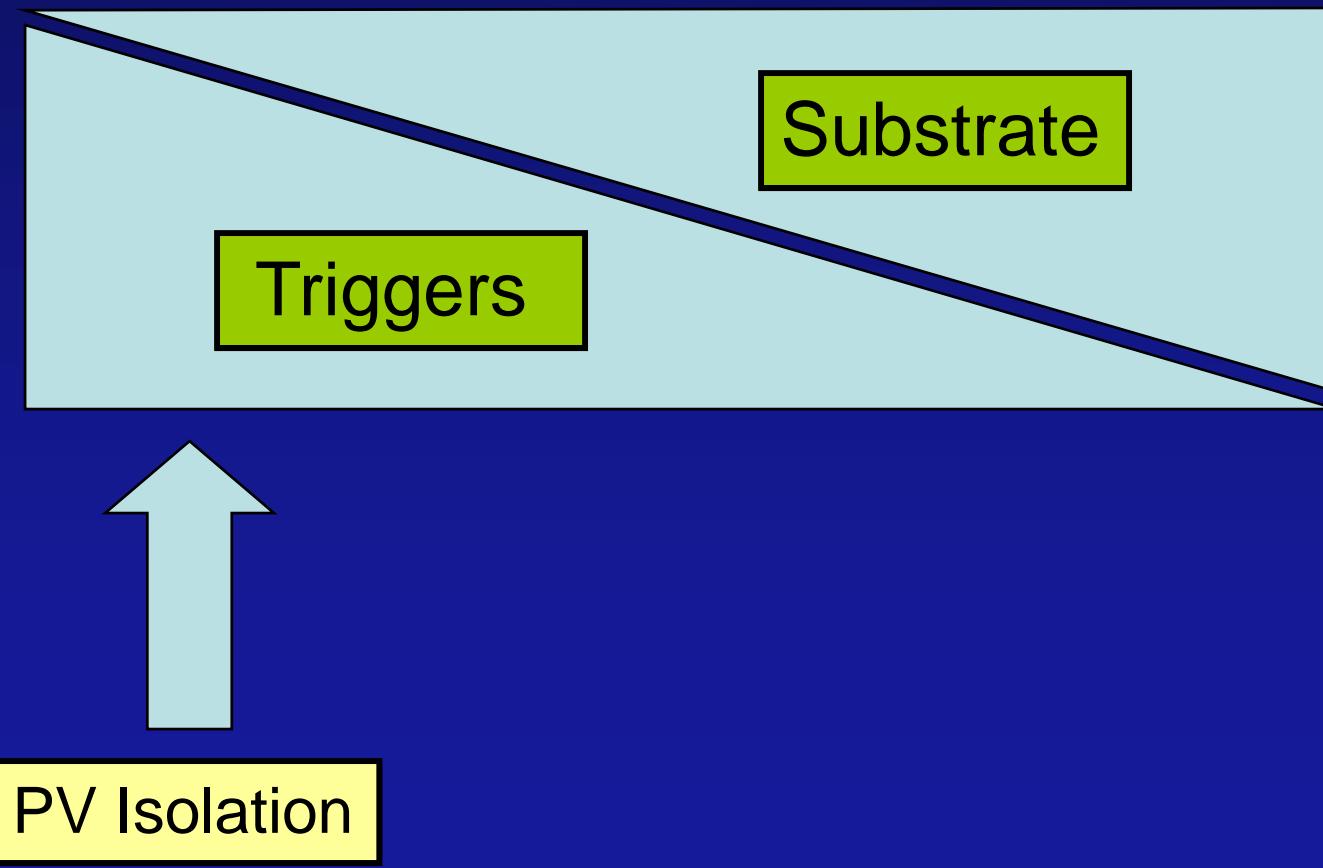
Linking AF Mechanism to Therapy



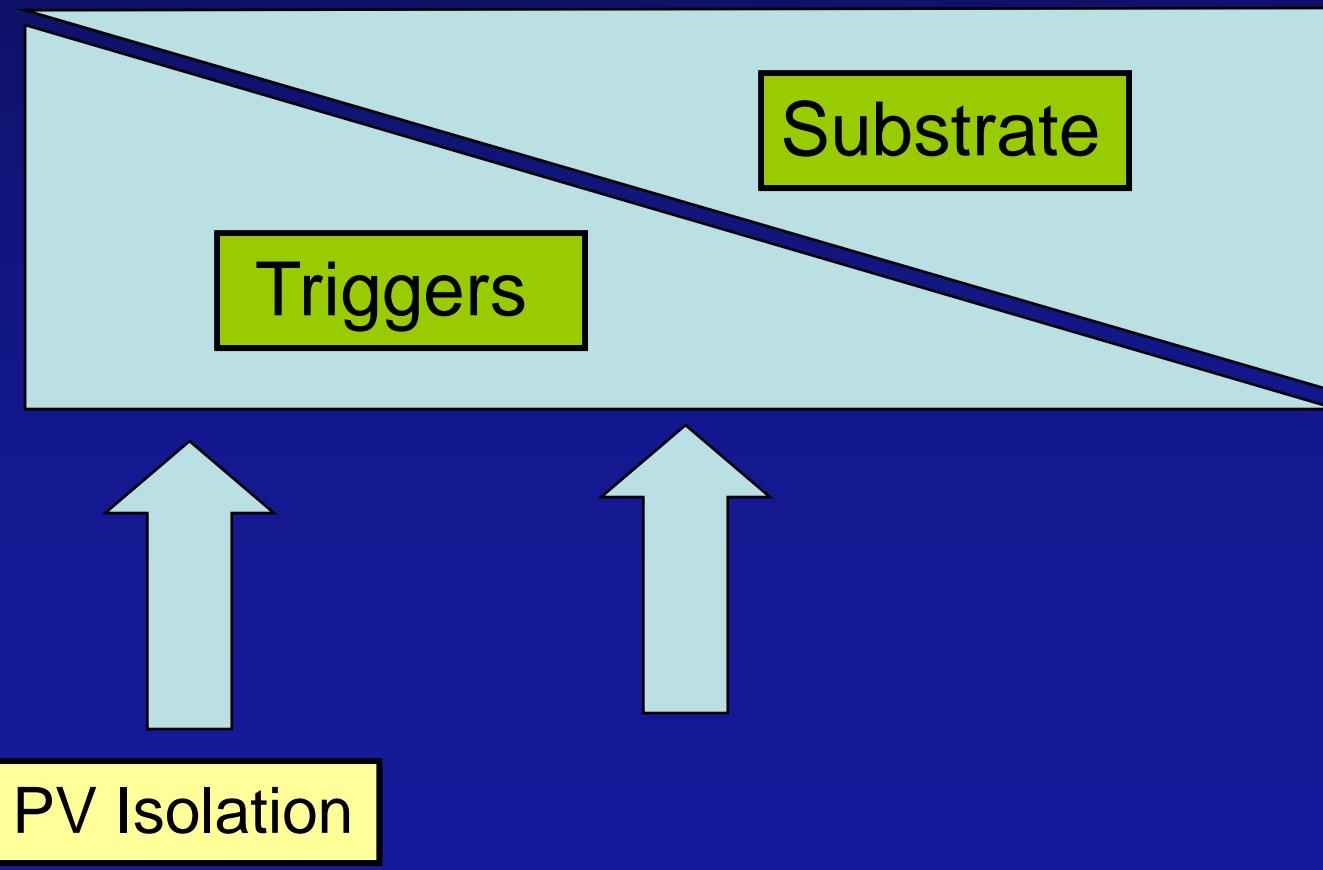
Linking AF Mechanism to Therapy



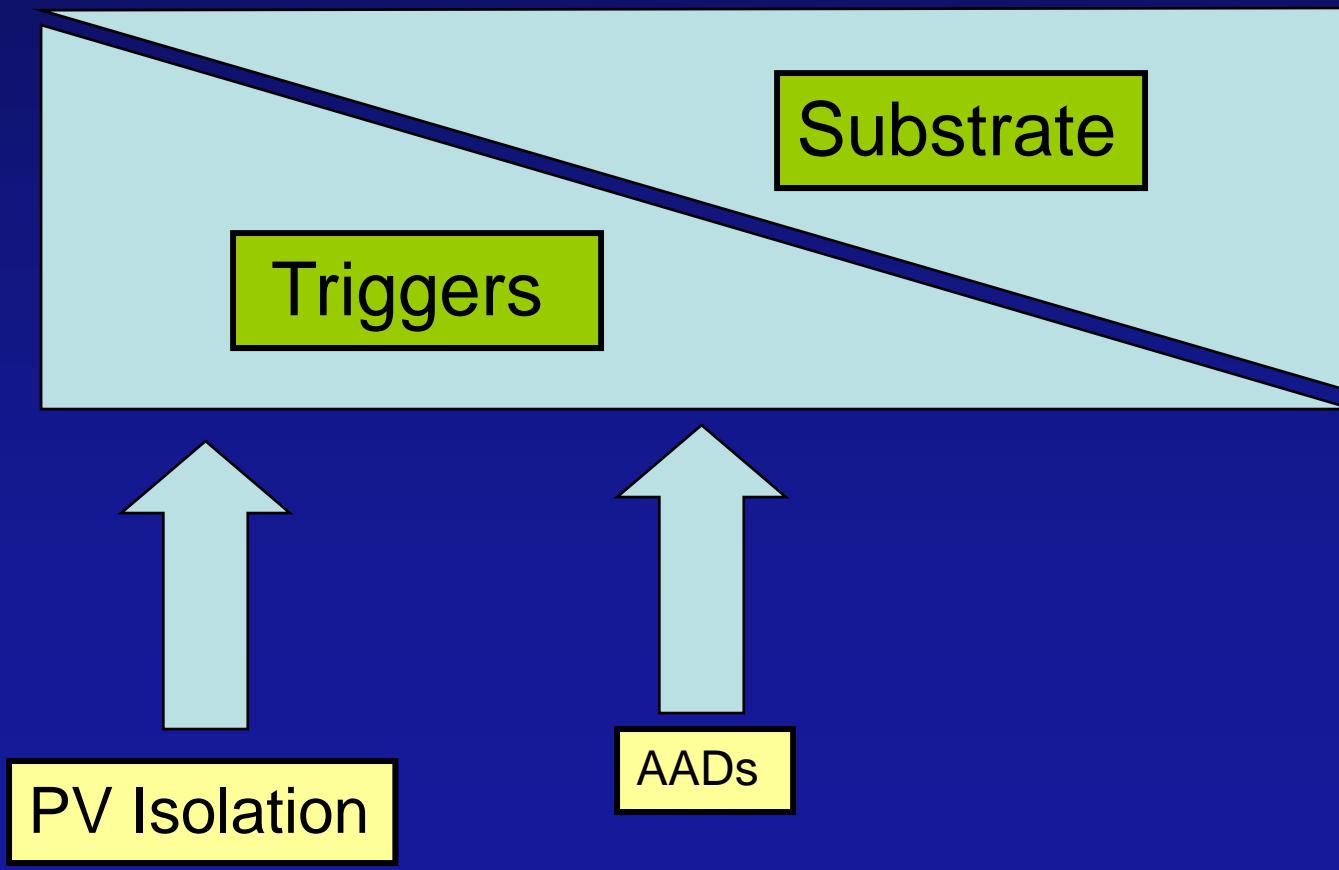
Linking AF Mechanism to Therapy



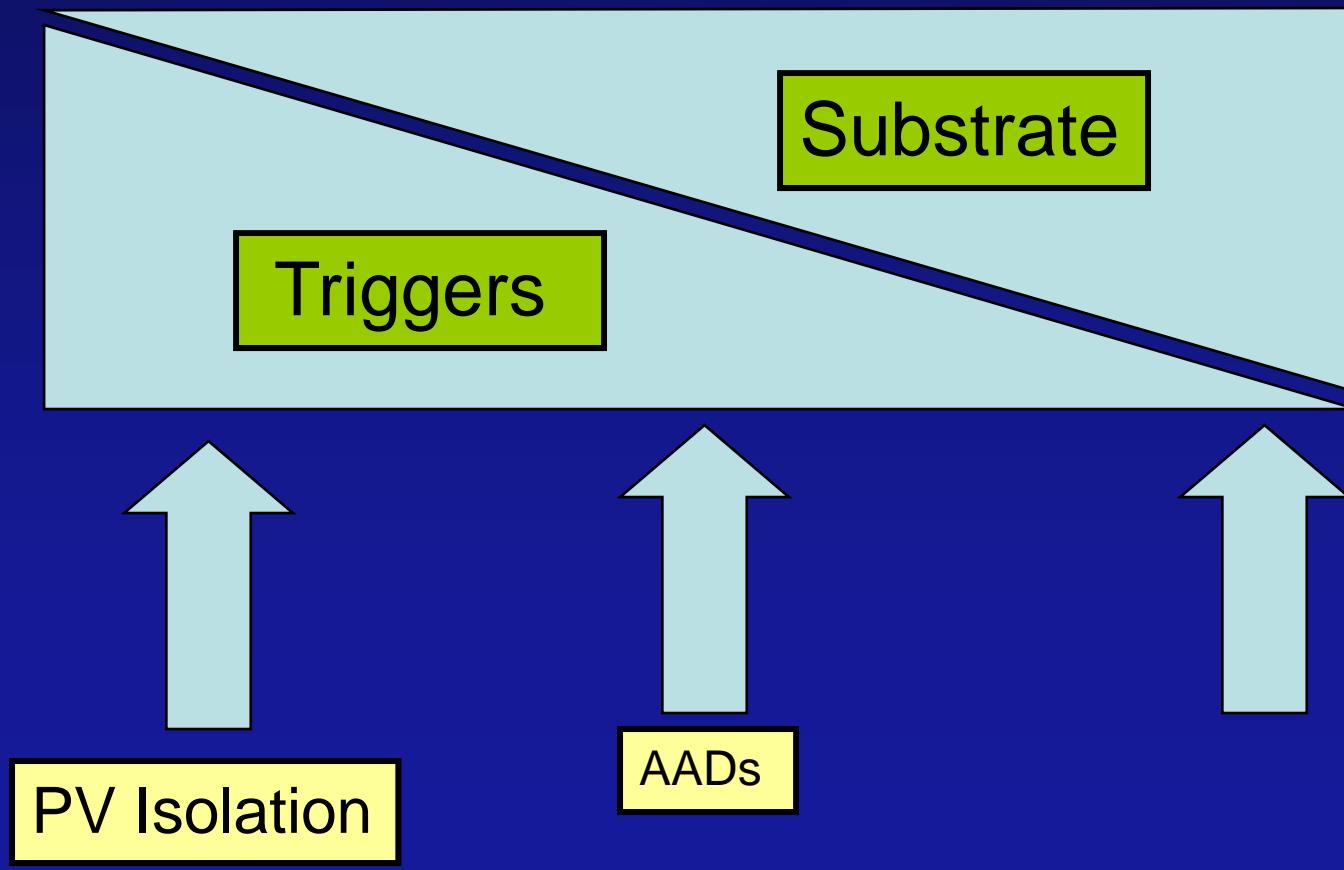
Linking AF Mechanism to Therapy



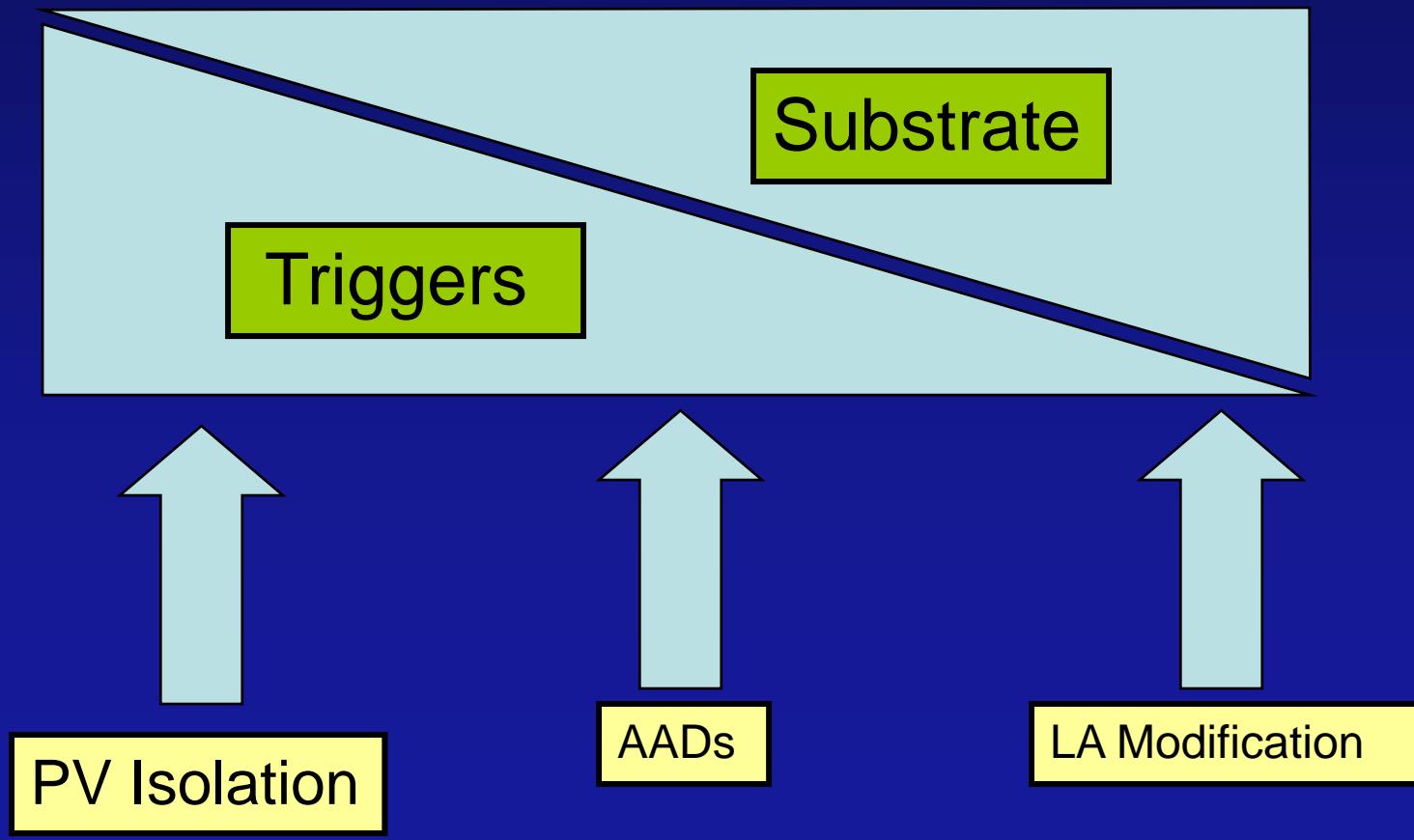
Linking AF Mechanism to Therapy



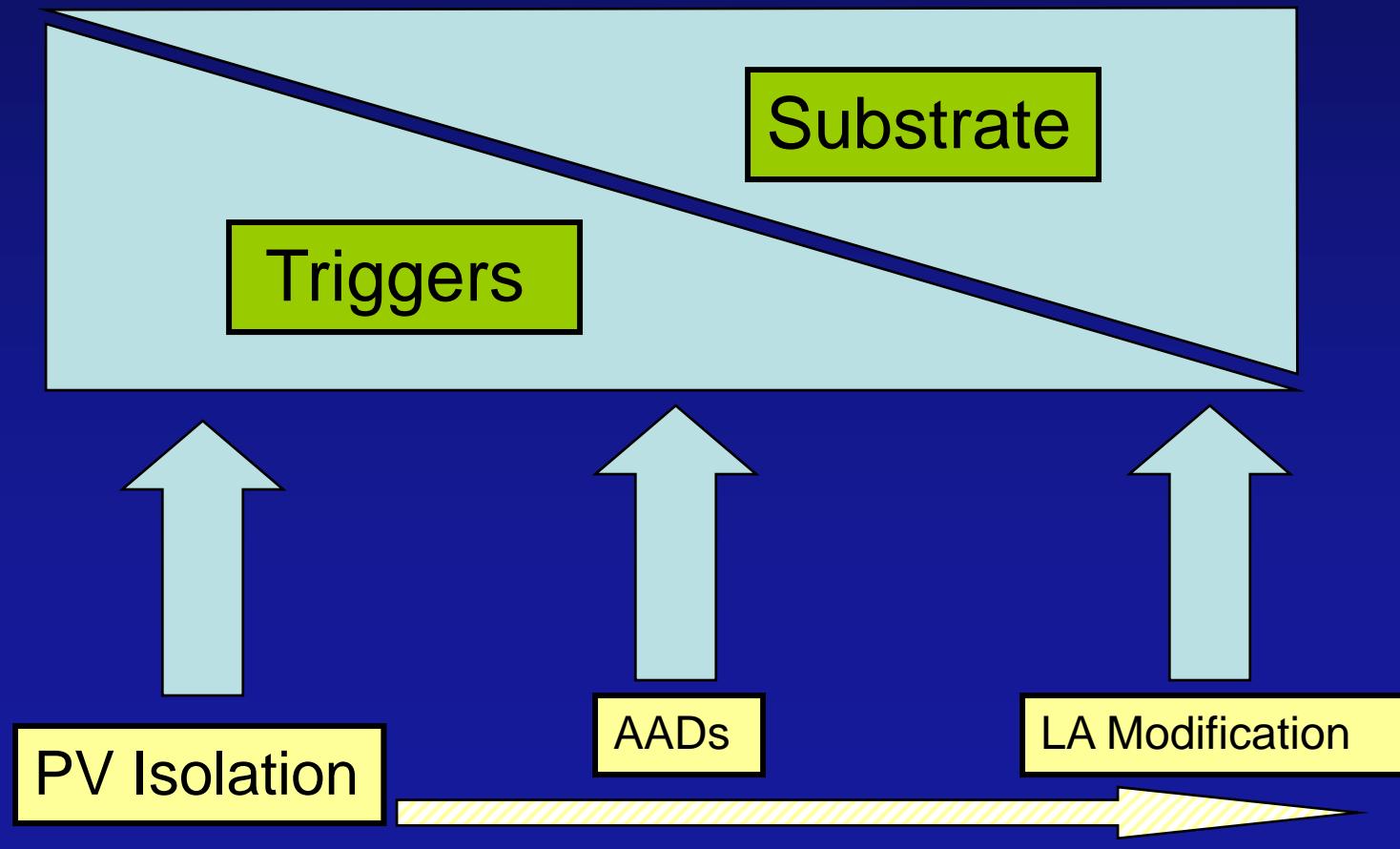
Linking AF Mechanism to Therapy



Linking AF Mechanism to Therapy



Linking AF Mechanism to Therapy



CHF-AF Treatment Algorithm

