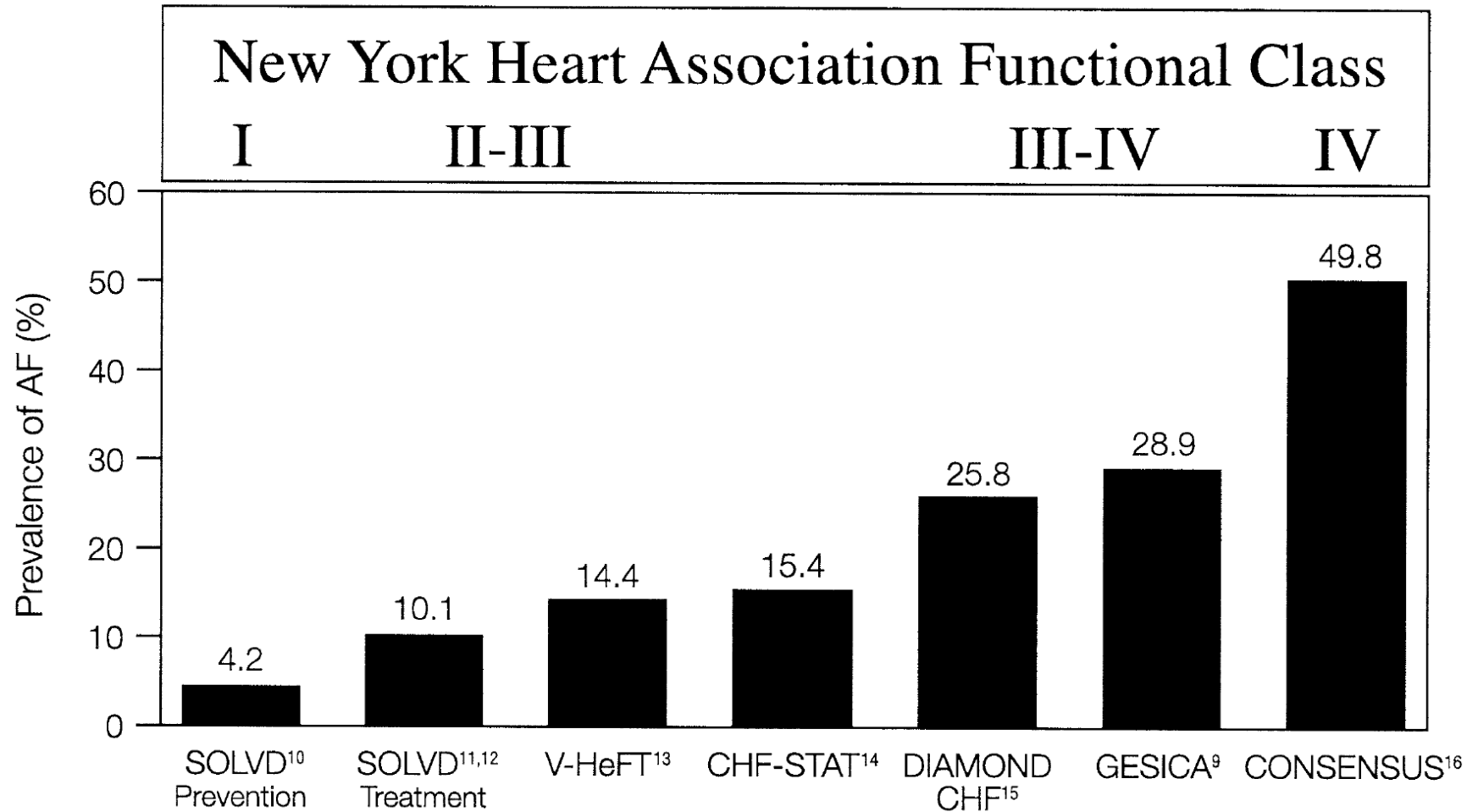


Afib and Heart Failure – what can we do?

Professor Frank Ruschitzka, MD, FESC, FRCP (Edinburgh)
Director, Heart Failure/Transplantation Clinic
University Clinic Zurich
Switzerland

Conflict of interest: Aventis, Bayer, Biomed, Biotronik, Boston Scientific, Cardiorientis, Merck, Pfizer, Novartis, Servier, St. Jude
Interest in Conflict: none

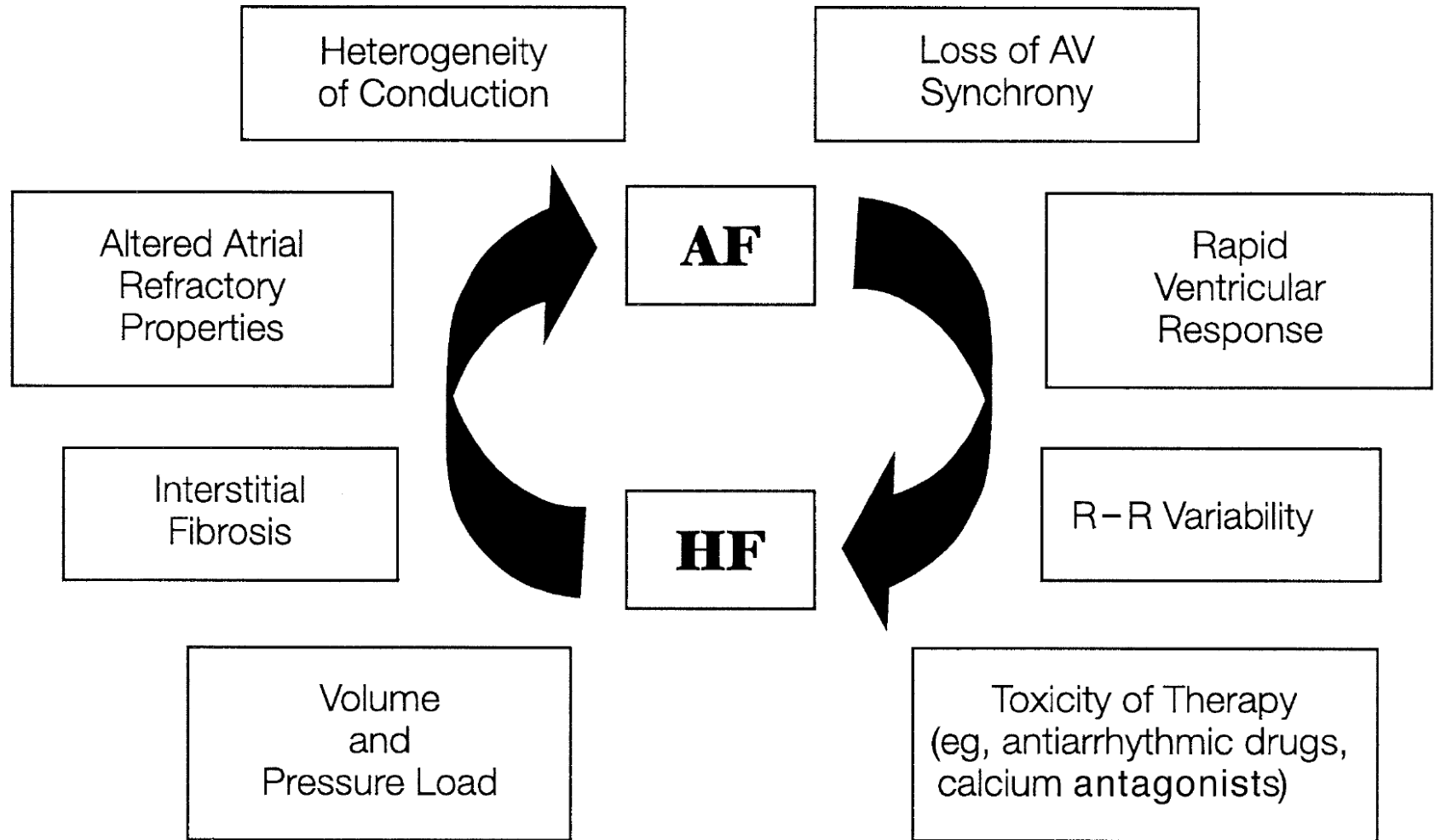
Prevalence of atrial fibrillation (AF) in several major heart failure trials



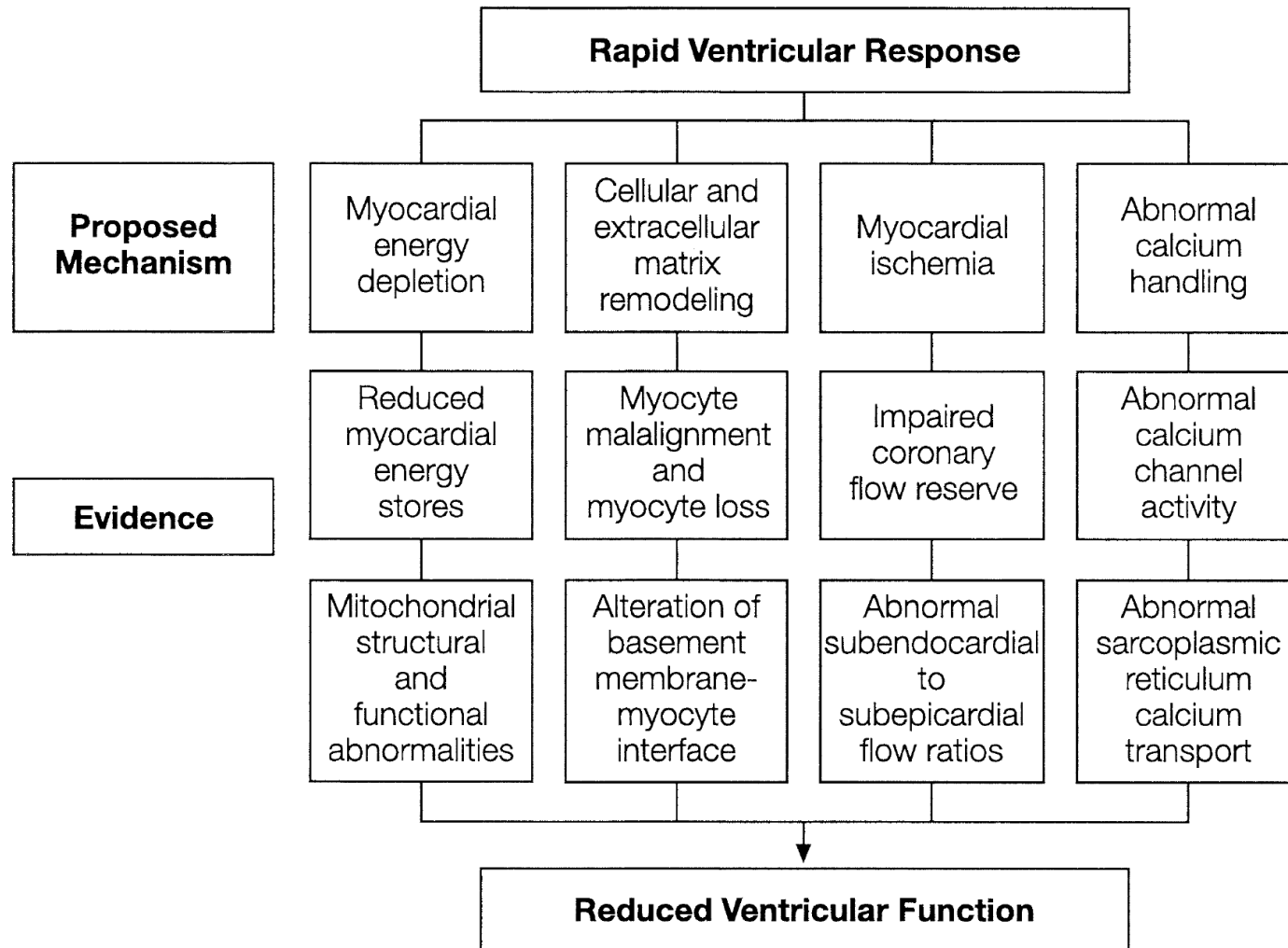


?

Atrial Fibrillation Begets Heart Failure



Proposed Mechanisms of tachycardia-induced cardiomyopathy



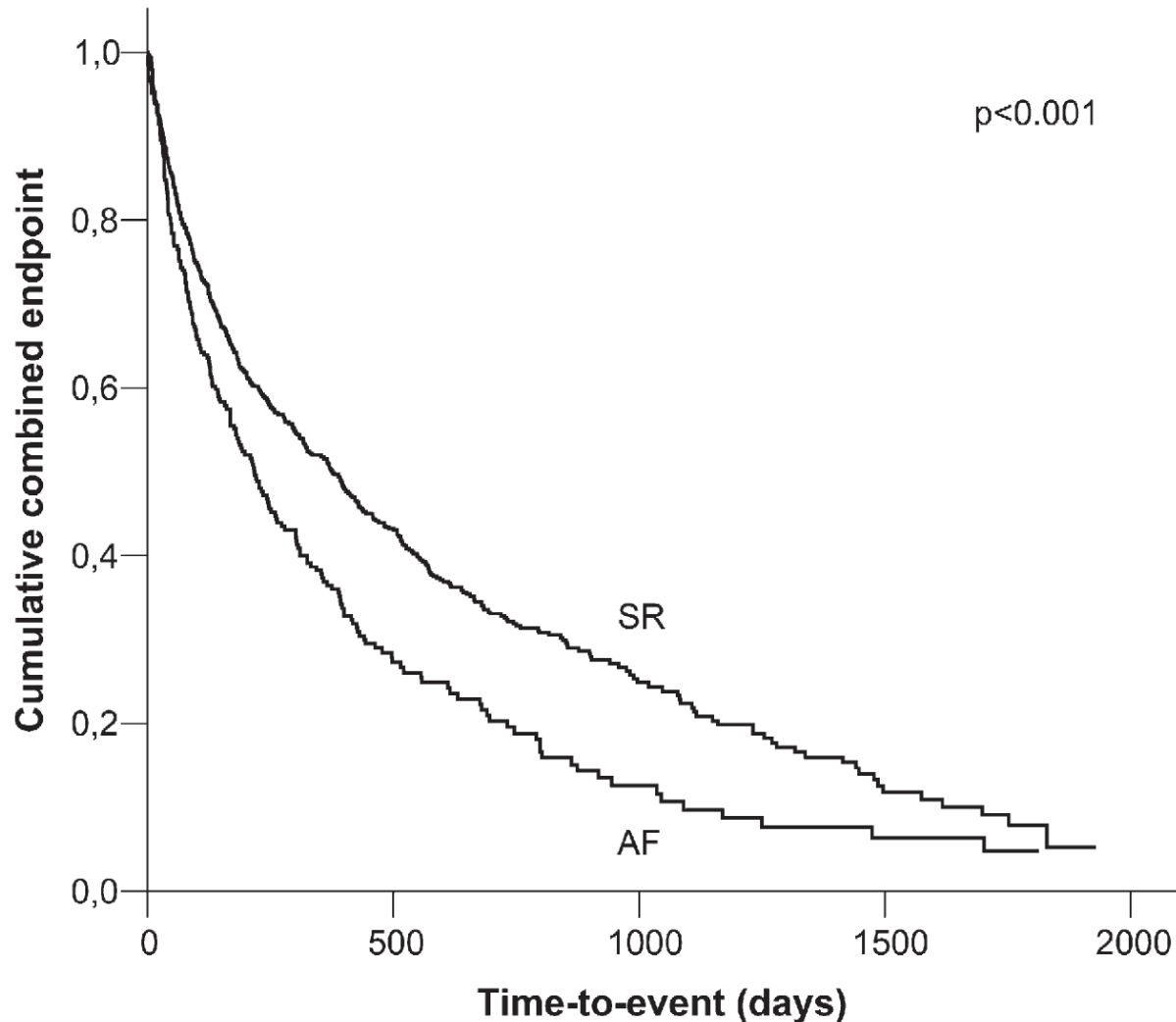
Prevalence and Prognostic significance of Afib in Patients with Heart Failure

	Sinus rhythm (<i>n</i> =750)	Atrial fibrillation (<i>n</i> =269)	<i>p</i> -value
Age (years)	70±11	74±9	<0.001
Sex (% females)	31.3	24.5	0.04
BMI (<i>n</i> =765)	26.7±5.1	27.0±4.9	ns
LVEF (%)	31.0±8.3	30.7±8.8	ns
NYHA III/IV (%) (<i>n</i> =298)	213(30.1)	85(33.2)	ns
Heart rate (bpm) (<i>n</i> =989)	72.7±14.7	74.8±15.6	ns
<i>P</i> -creatinine (μmol/l) (<i>n</i> =827)	108±44	116±52	0.04
Diastolic blood pressure (mm Hg) (<i>n</i> =995)	74.0±13.8	76.1±14.0	0.03
Systolic blood pressure (mm Hg) (<i>n</i> =996)	129.7±25.5	129.0±22.8	ns
Bundle branch block (%) (<i>n</i> =858)	36.7	25.1	0.001

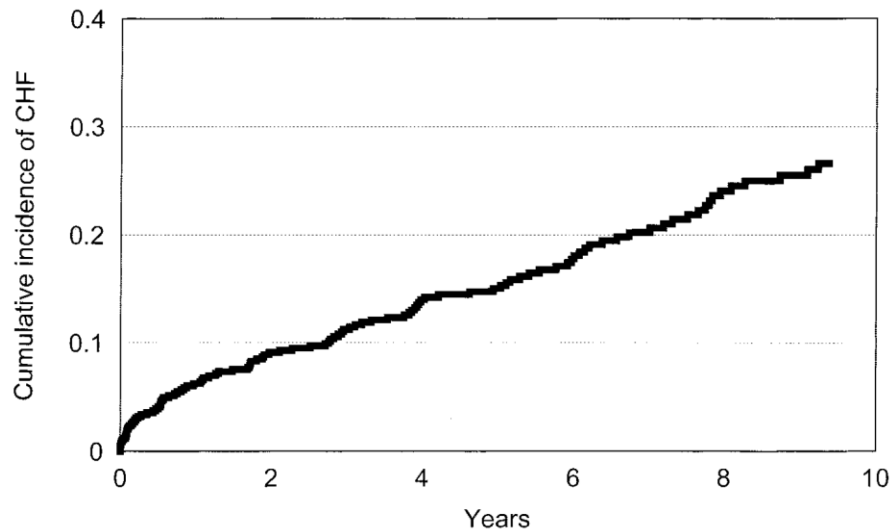
- At baseline 26.4% of CHF pts have Afib

- 18.7 % developed new-onset Afib

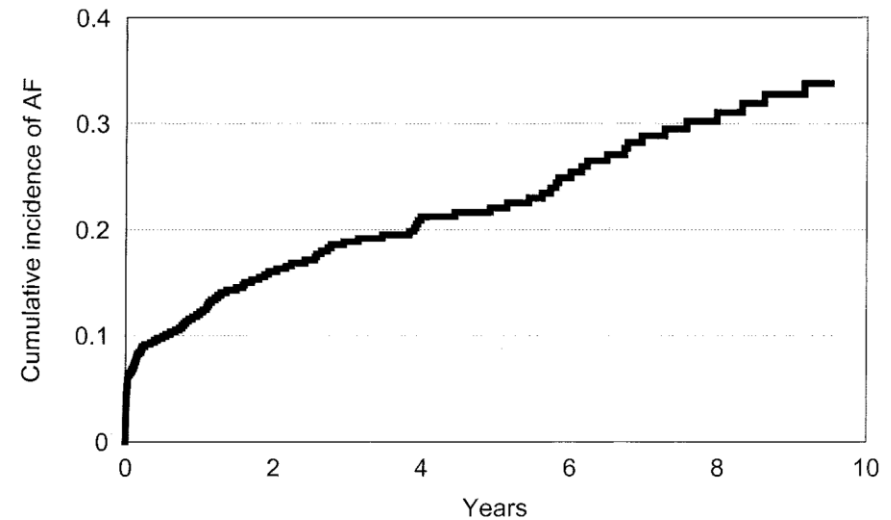
Cumulative all-cause mortality or all-cause hospitalisation for patients with baseline atrial fibrillation (AF) and sinus rhythm (SR)



Unadjusted Cumulative Incidence of First CHF in Individuals with AF or vice versa in the Framingham Heart Study



**First CHF in individuals
with AF**

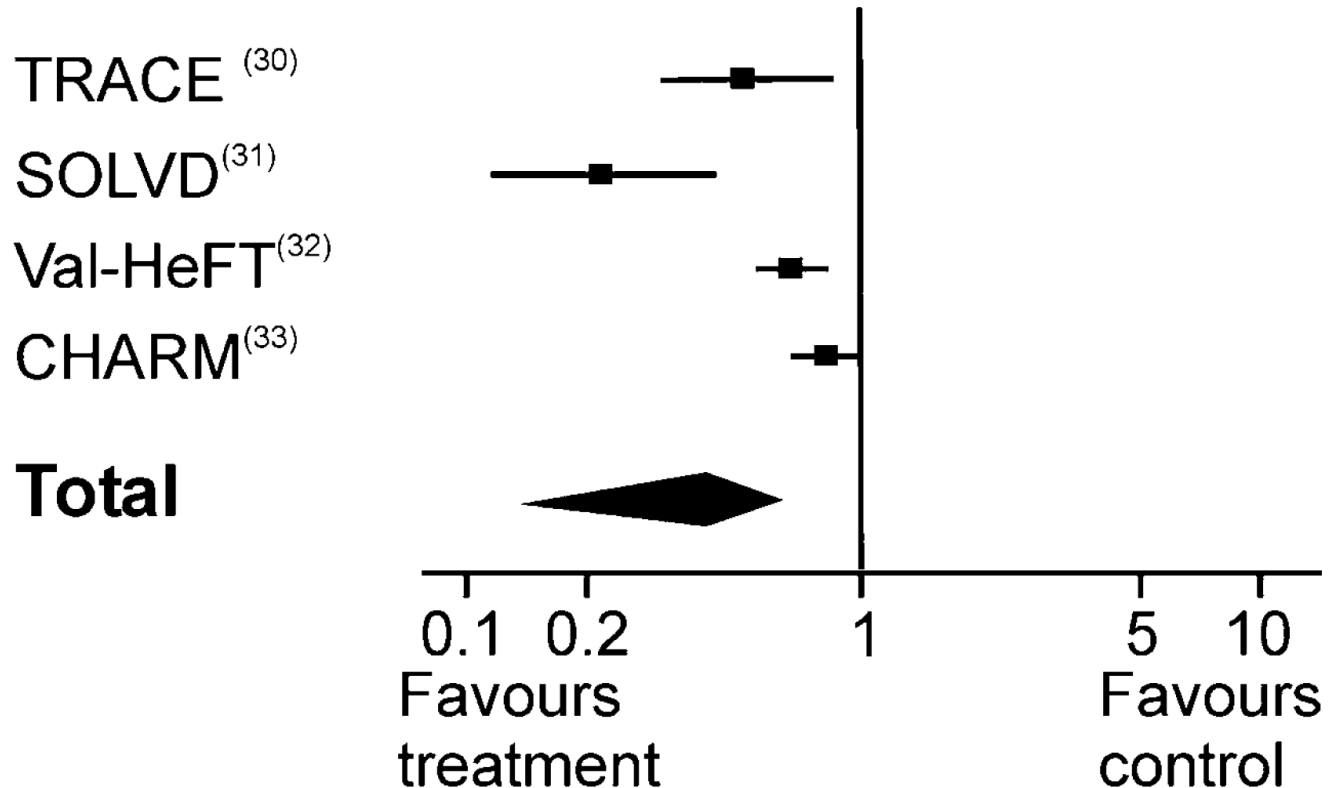


**First AF in individuals
with CHF**

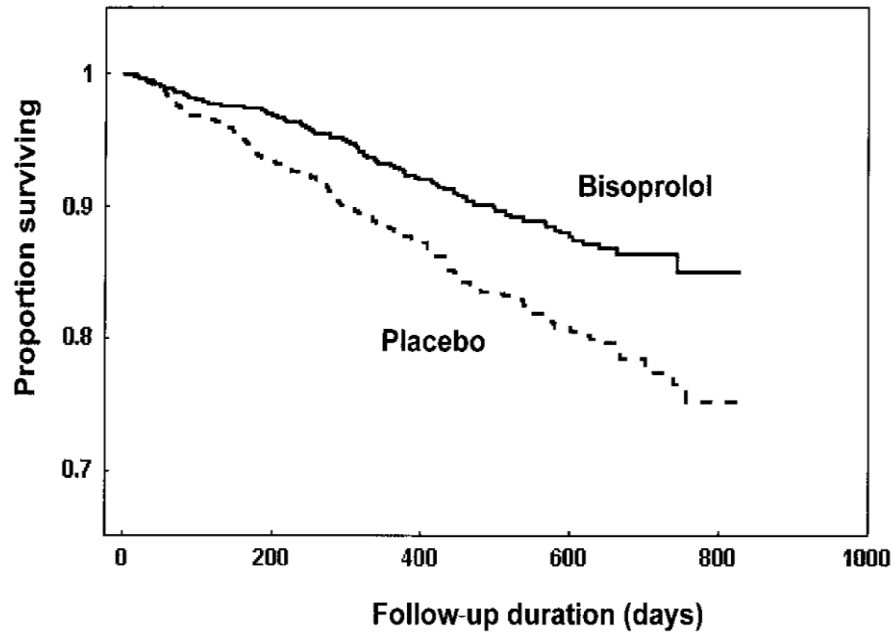
Prevention of AFib by ACE inhibitors and ARBs in Heart Failure

Heart Failure Trial

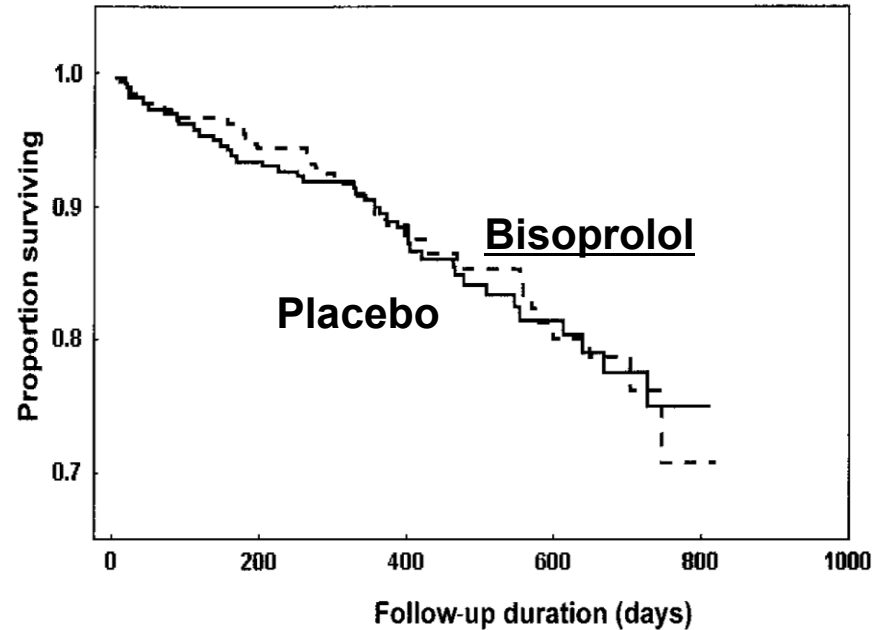
RR
(95% CI random)



CIBIS II Survival Curves in Patients with Atrial Fibrillation or Sinus Rhythm at Baseline

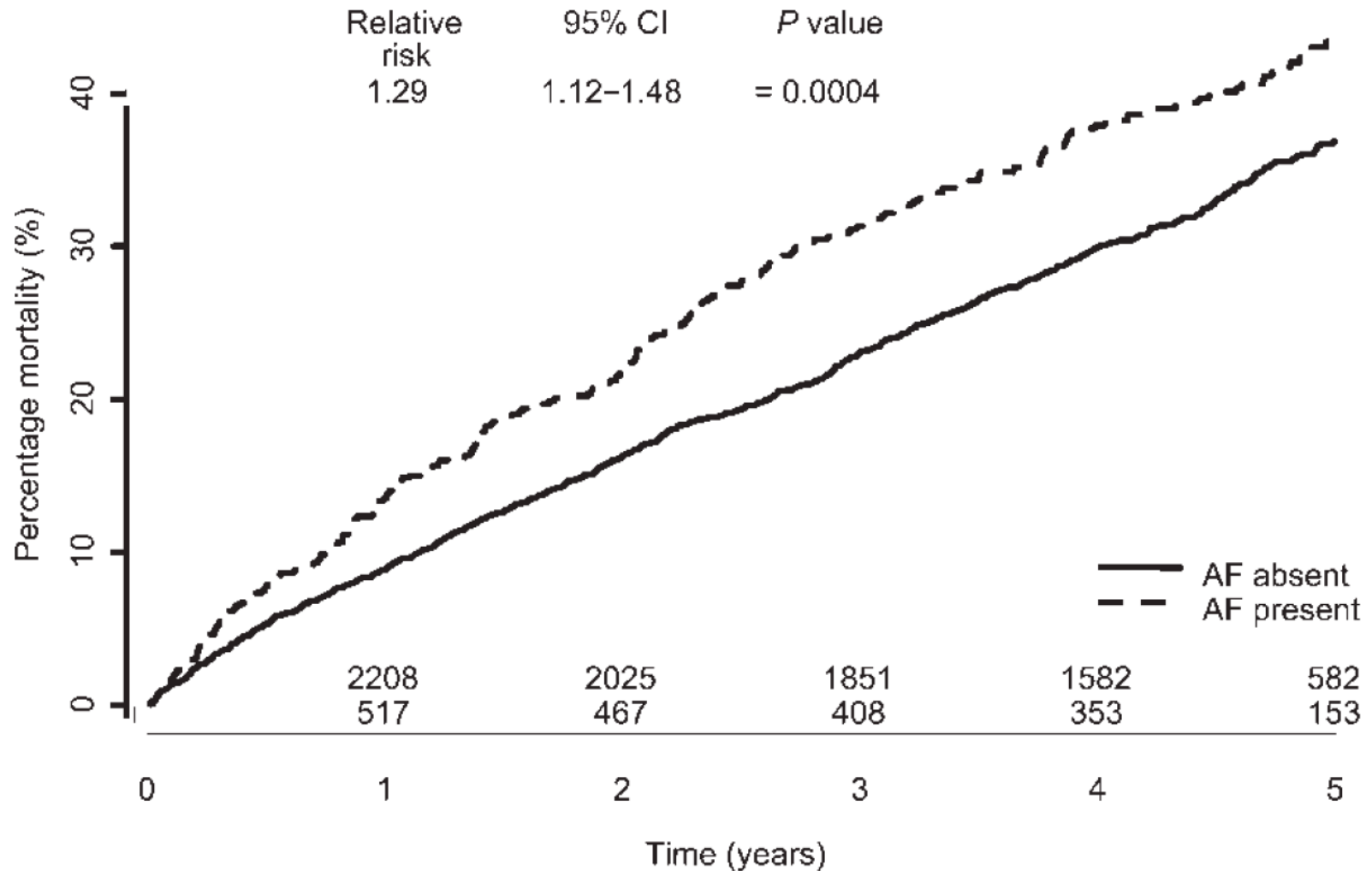


Sinus Rhythm at baseline

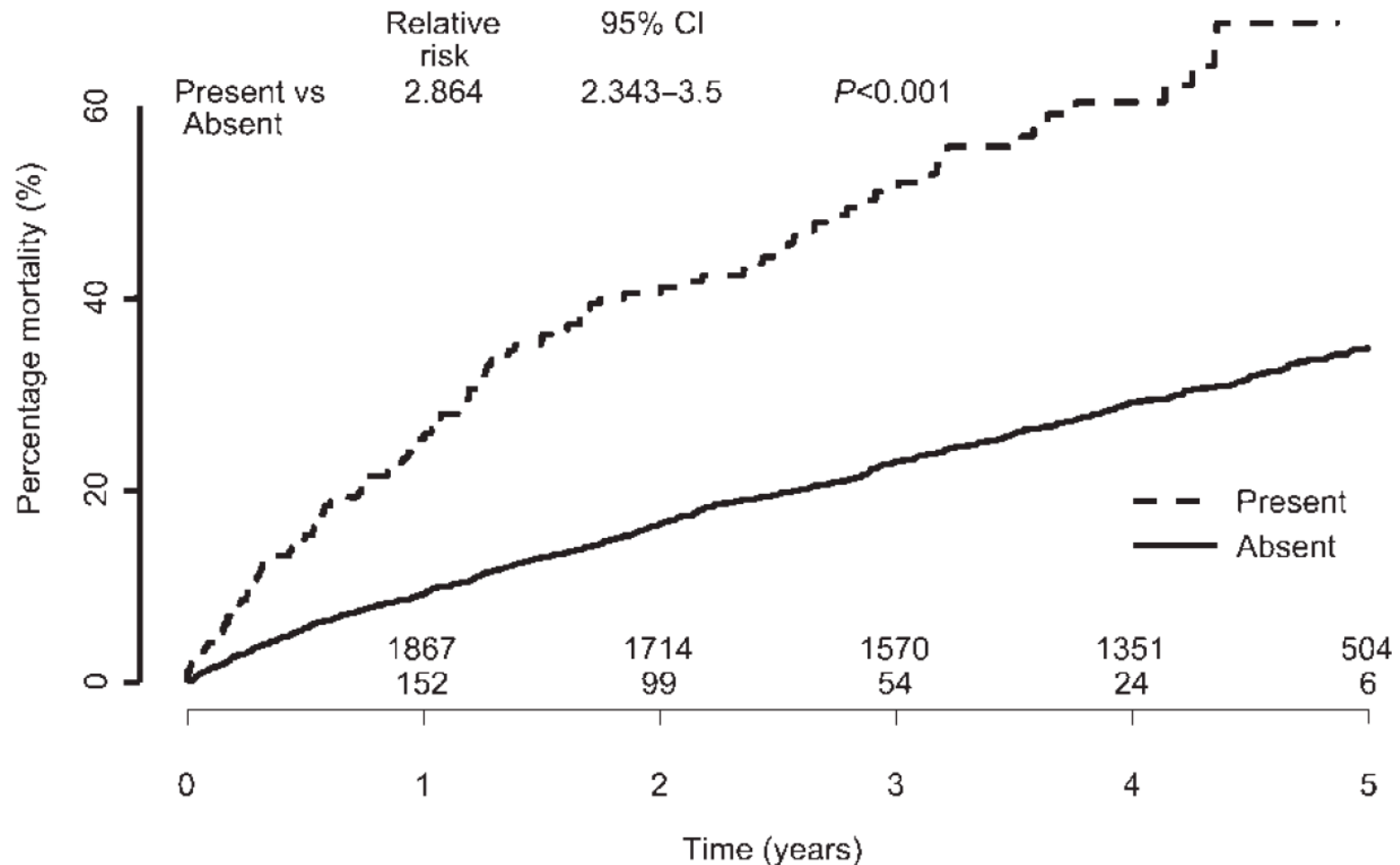


Afib at baseline

All-cause mortality by Baseline Atrial Fibrillation in Patients with CHF: Lessons from COMET



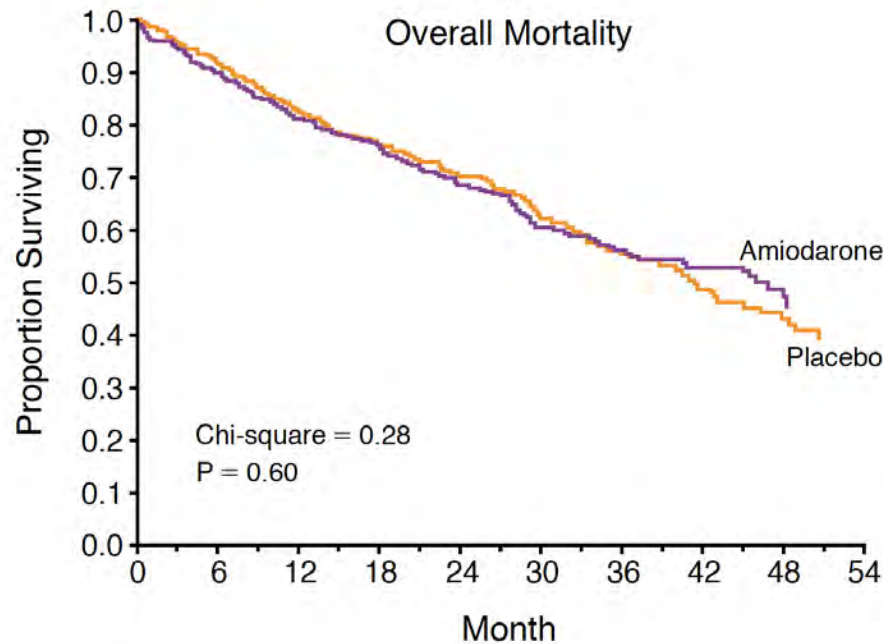
Mortality following **New Onset AF** in Patients with Sinus Rhythm at Baseline in COMET



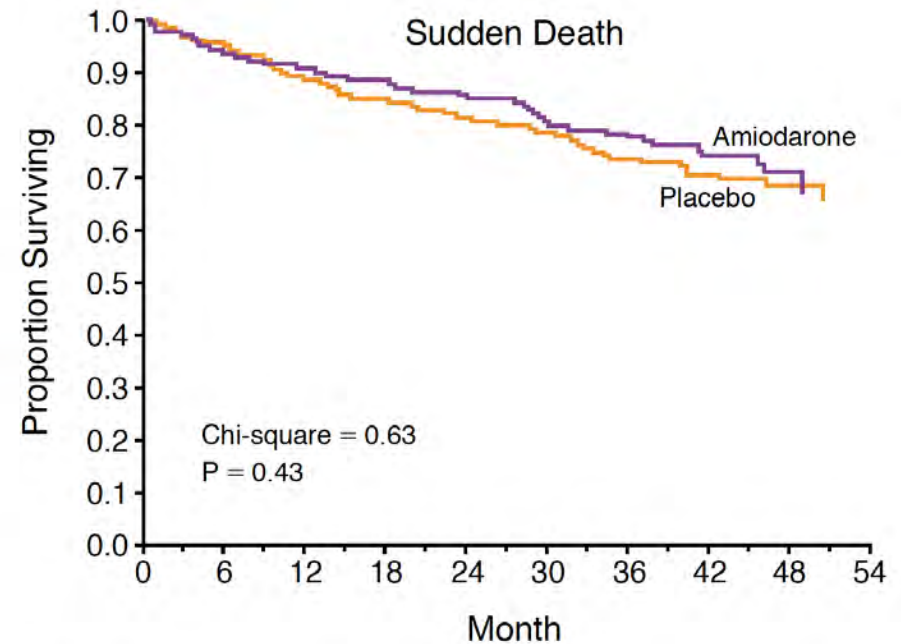
Multivariate Analysis of Risk of All-Cause Mortality in Patients with Afib vs No Afib in COMET

	RR	95% CI	P-value
Carvedilol vs. metoprolol	0.836	0.74, 0.945	0.0042
Increasing age	1.036	1.029, 1.043	<0.001
Female vs. male	0.868	0.738, 1.02	0.0855
Increasing systolic BP	0.992	0.988, 0.995	<0.001
Increasing LVEF	0.98	0.971, 0.988	<0.001
IHD vs. rest	1.326	1.154, 1.522	0.0001
NYHA III vs. NYHA II	1.439	1.259, 1.645	<0.001
NYHA IV vs. NYHA II	1.827	1.392, 2.398	<0.001
Previous angina	0.939	0.809, 1.09	0.4078
Increasing sodium	0.941	0.925, 0.957	<0.001
Increasing creatinine	1.002	1.001, 1.003	<0.001
Diuretic dose	1.366	1.183, 1.578	<0.001
41–120 vs. ≤40 mg			
Diuretic dose	1.633	1.374, 1.939	<0.001
>120 vs. <40 mg			
AF vs. No AF	1.069	0.921, 1.242	0.3811

Amiodarone in Patients with Congestive Heart Failure and Asymptomatic Ventricular Arrhythmia: Results from CHF-STAT



Amiodarone	336	260	175	101	33
Placebo	338	263	178	95	39



Amiodarone	336	260	175	101	33
Placebo	338	263	178	95	39

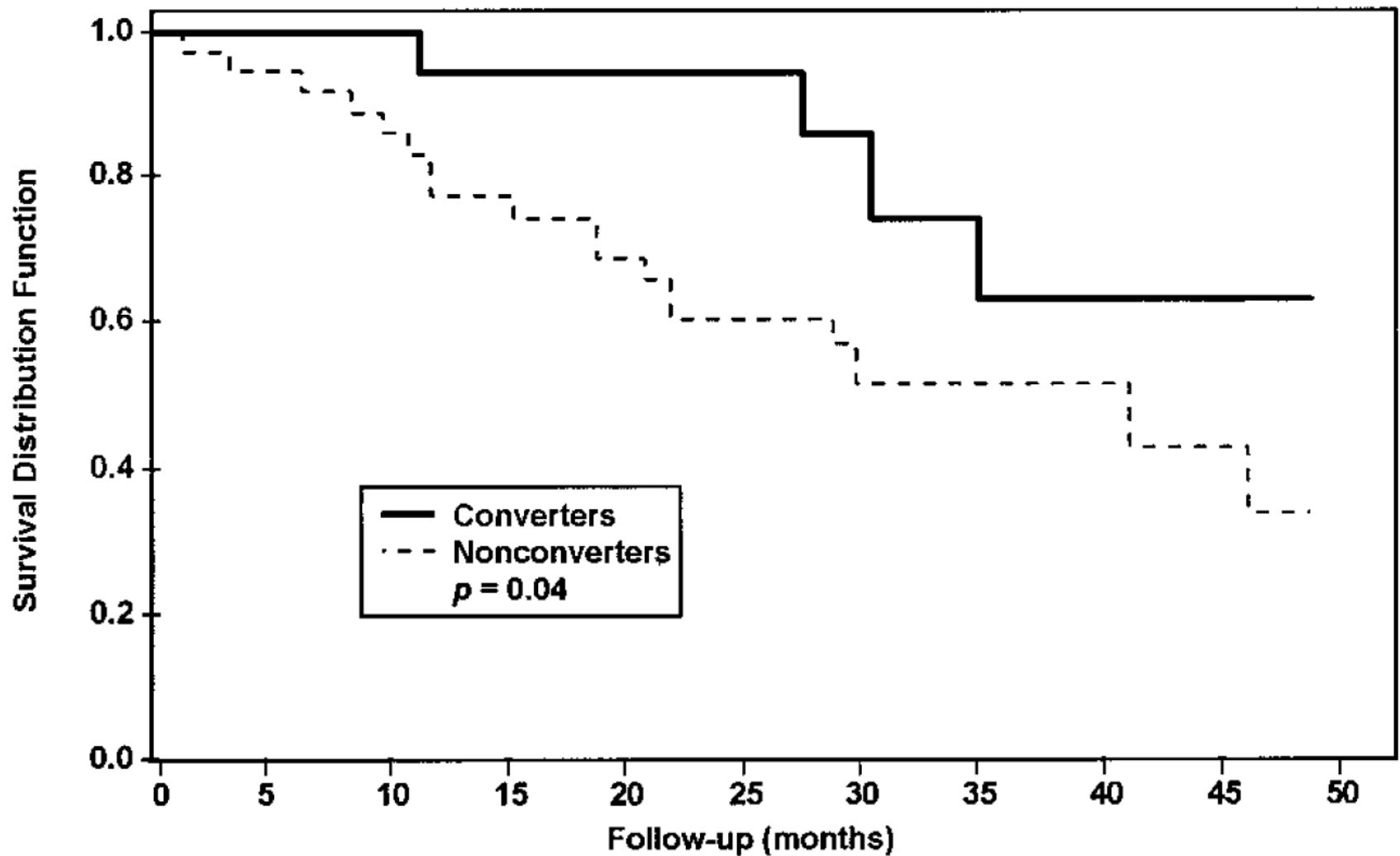
Singh NEJM 1995

Veterans Affairs Congestive Heart Failure Survival Trial of Antiarrhythmic Therapy

Onset of New AF With Amiodarone vs Placebo During 4-Year Follow-Up in CHF-STAT

	Amiodarone (n=330)	Placebo (n=337)
Sinus rhythm	268	263
AF at randomization	51	52
AF Always	35	48
Converted to NSR	16	4*
AF New-onset	11	22†

Survival in Heart Failure Patients with AFib who Converted vs Those Who did not Convert



The Blue Man



Enseleit Circulation 2006

Meet Henry Kissinger Baritone



The absence of
alternatives clears the
mind marvelously

Henry Kissinger (1923 -)

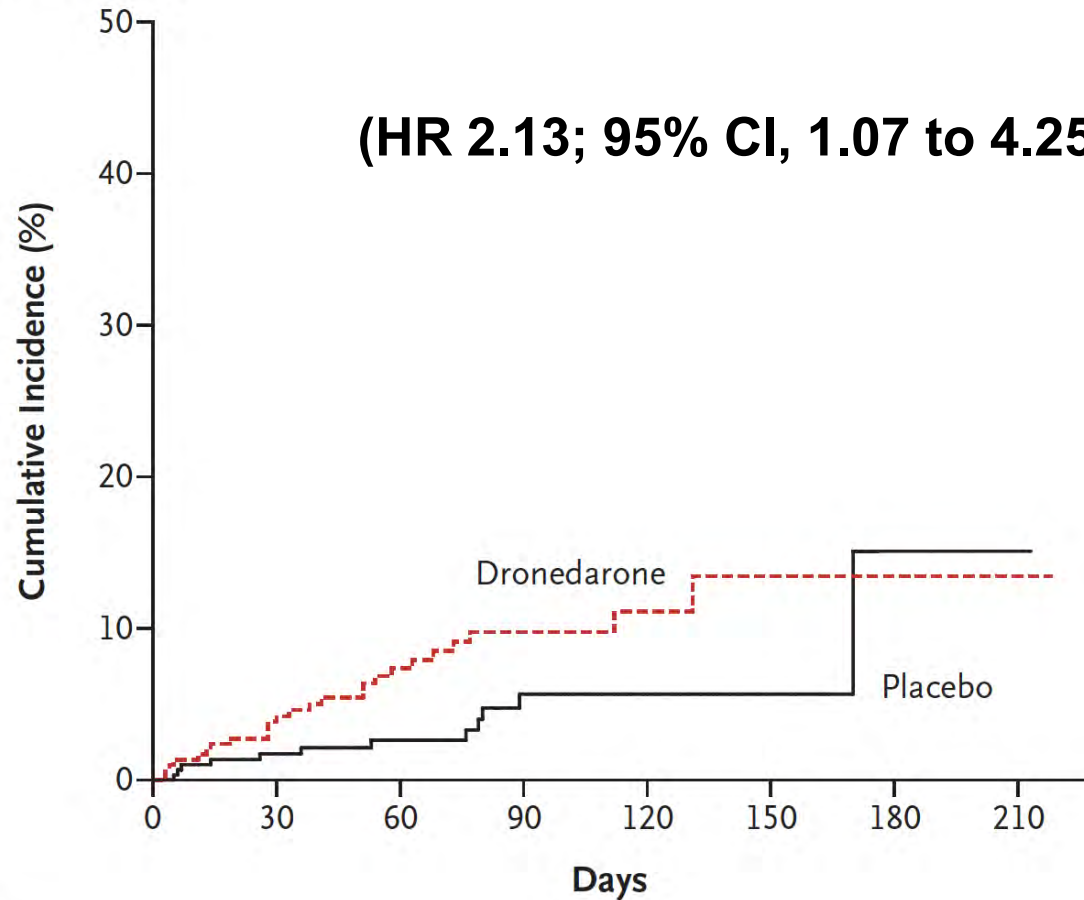
Dronedarone in Patients with Severe Heart Failure:

Results from **ANDROMEDA**

Characteristic	Dronedarone Group (N=310)	Placebo Group (N=317)
Mean blood pressure — mm Hg		
Systolic	120	122
Diastolic	73	74
Mean heart rate — beats/min	78	81
Atrial fibrillation at randomization — no. (%)	72 (23.2)	85 (26.8)
Medications at randomization — no. (%)		
ACE inhibitor or angiotensin-receptor blocker	274 (88.4)	267 (84.2)
Beta-blocker	192 (61.9)	192 (60.6)
Spironolactone	131 (42.3)	124 (39.1)
Diuretic (other than spironolactone)	288 (92.9)	302 (95.3)
Digitalis	96 (31.0)	101 (31.9)
Anticoagulant	92 (29.7)	102 (32.2)
Treatment with ICD — no. (%)	4 (1.3)	6 (1.9)
NYHA functional class — no. (%)		
I	0	0
II	131 (42.3)	121 (38.2)
III	173 (55.8)	183 (57.7)
IV	6 (1.9)	13 (4.1)

ANDROMEDA: Increased Mortality after Dronedarone Therapy for Severe Heart Failure

B All-Cause Mortality



No. at Risk

Placebo	317	256	181	103	50	18	6	1
Dronedarone	310	257	174	104	59	22	5	1

ANDROMEDA: Increased Mortality after Dronedarone Therapy for Severe Heart Failure

Table 2. Cause of Death.

Cause	Dronedarone Group (N = 310)	Placebo Group (N = 317)
	<i>no. (%)</i>	
Cardiovascular	24 (7.7)	9 (2.8)
Myocardial infarction	0	2 (0.6)
Progressive heart failure	10 (3.2)	2 (0.6)
Documented arrhythmia	6 (1.9)	2 (0.6)
Other cardiovascular cause	3 (1.0)	0
Presumed cardiovascular cause	5 (1.6)	3 (0.9)
Arrhythmia or sudden death*	10 (3.2)	6 (1.9)
Noncardiovascular	1 (0.3)	3 (0.9)
Total	25 (8.1)	12 (3.8)

ANDROMEDA: Increased Mortality after Dronedarone Therapy for Severe Heart Failure

Table 3. Incidence of Death According to Subgroup.*

Subgroup	Dronedarone Group (N=310)	Placebo Group (N=317)	Hazard Ratio for Death in the Dronedarone Group (95% CI)	P Value for Interaction
<i>no. of deaths/total no. of patients</i>				
Baseline estimated GFR (ml/ min/1.73 m ²) [†]				0.09
<50	20/148	5/130	3.32 (1.25–8.87) [‡]	
≥50	4/155	6/180	0.89 (0.25–3.20)	
Baseline wall-motion index [§]				0.04
<1.0	15/144	4/180	4.61 (1.53–13.9) [‡]	
≥1.0	10/165	8/136	1.05 (0.42–2.67)	
Baseline NYHA class				0.33
II	7/131	5/121	1.28 (0.41–4.03)	
>II	18/179	7/196	2.77 (1.16–6.63) [‡]	
ACE inhibitor or ARB				0.52
Yes	18/274	9/267	1.96 (0.88–4.37)	
No	7/36	3/50	3.40 (0.88–13.2)	
Beta-blocker (excluding sotalol)				0.72
Yes	16/192	7/191	2.36 (0.97–5.75)	
No	9/118	5/126	1.82 (0.61–5.44)	
Digitalis				0.13
Yes	13/96	3/101	4.25 (1.21–14.9) [‡]	
No	12/214	9/216	1.34 (0.57–3.19)	
Spironolactone				0.93
Yes	12/131	5/124	2.19 (0.77–6.22)	
No	13/179	7/193	2.01 (0.80–5.04)	
Ischemic heart disease				0.23
Yes	17/206	10/201	1.61 (0.74–3.72)	
No	8/104	2/116	9.03 (1.13–72.2) [‡]	

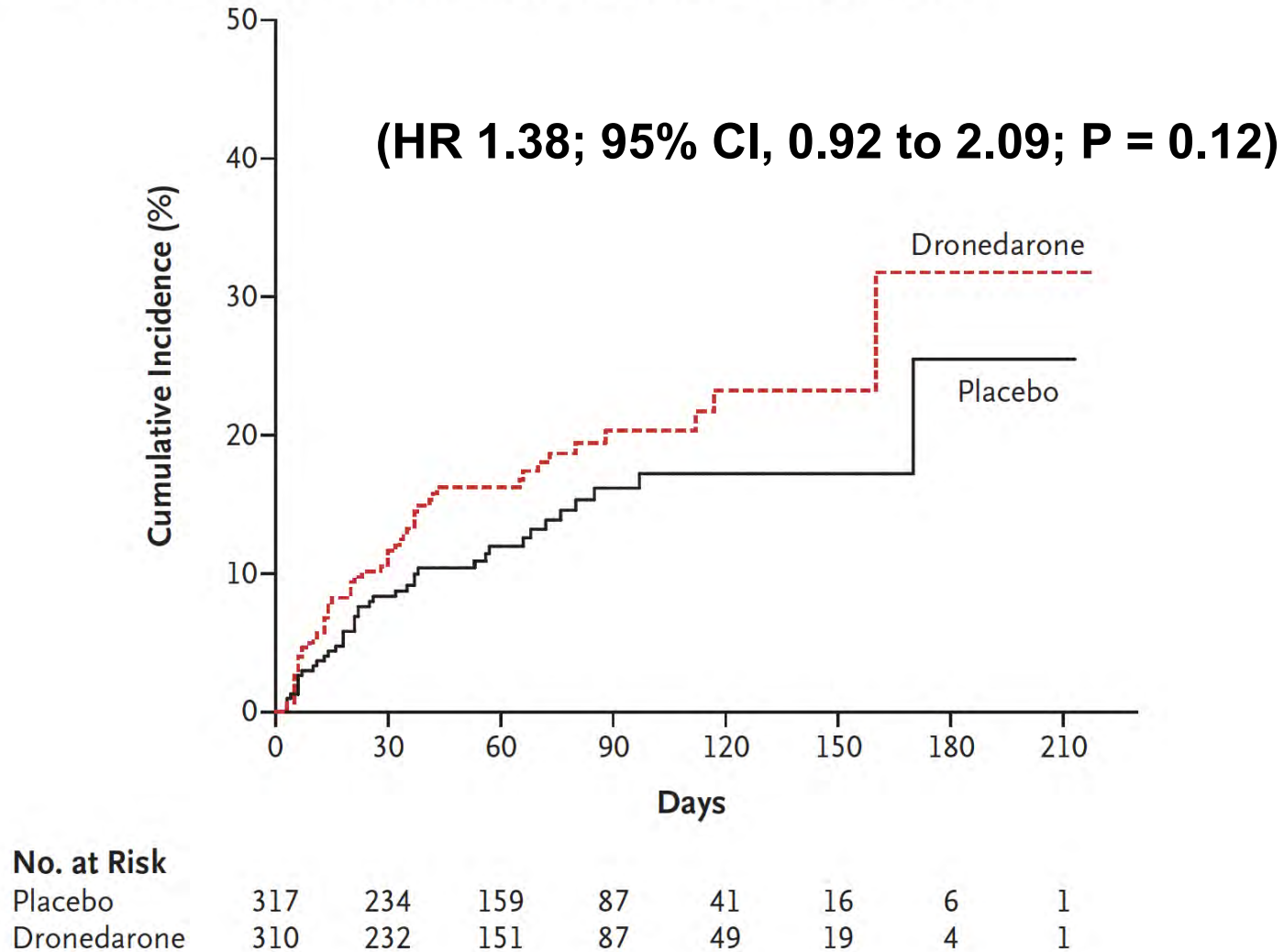
ANDROMEDA: Increased Mortality after Dronedarone Therapy for Severe Heart Failure

Table 4. Patients with Serious Adverse Events, Excluding Events Resulting in Death, during the Treatment Period.*

Adverse Event	Dronedarone Group (N = 310)	Placebo Group (N = 317)
	<i>no (%)</i>	
Any event	115 (37.1)	109 (34.4)
Any cardiac event	68 (21.9)	52 (16.4)
Cardiac failure	31 (10.0)	26 (8.2)
Angina pectoris	7 (2.3)	7 (2.2)
Myocardial infarction	2 (0.6)	4 (1.3)
Ventricular fibrillation	1 (0.3)	3 (0.9)
Ventricular tachycardia	6 (1.9)	2 (0.6)
Noncardiac events		
Increase in serum creatinine	8 (2.6)	0†
Any infection	9 (2.9)	9 (2.8)
Any gastrointestinal event	8 (2.6)	7 (2.2)
Any respiratory event	14 (4.5)	14 (4.4)
Surgical procedures		
Coronary-artery bypass	0	6 (1.9)
Coronary angioplasty	0	1 (0.3)
ICD placement	0	1 (0.3)

Dronedarone in Patients with Severe Heart Failure: Results from **ANDROMEDA**

A All-Cause Mortality or Hospitalization for Worsening Heart Failure



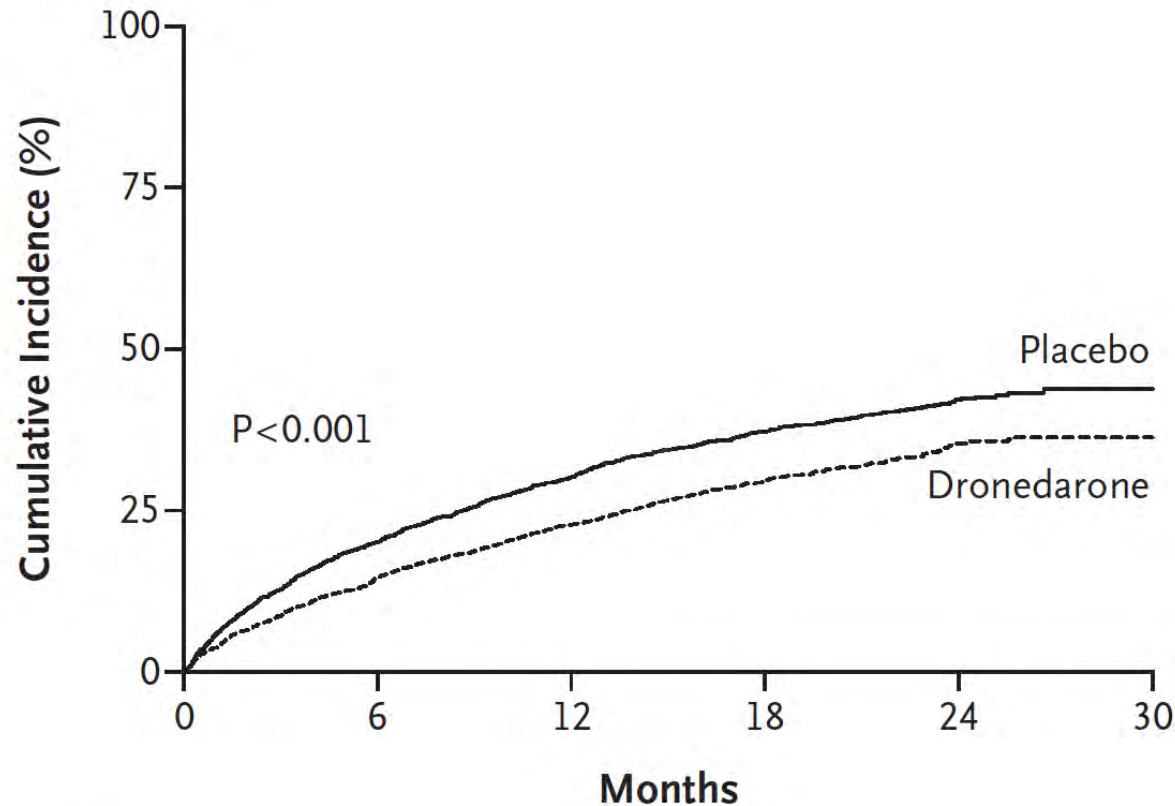
ATHENA: Effect of Dronedarone on Cardiovascular Events in Atrial Fibrillation

Table 1. Baseline Characteristics of the Study Patients.*

Characteristic	Dronedarone (N = 2301)	Placebo (N = 2327)	All (N = 4628)
Age			
Mean $\pm$ SD — yr	71.6 $\pm$ 8.9	71.7 $\pm$ 9.0	71.6 $\pm$ 9.0
<65 yr — no. (%)	431 (18.7)	442 (19.0)	873 (18.9)
65 to <75 yr — no. (%)	923 (40.1)	907 (39.0)	1830 (39.5)
$\geq$ 75 yr — no. (%)	947 (41.2)	978 (42.0)	1925 (41.6)
Female sex — no. (%)	1131 (49.2)	1038 (44.6)	2169 (46.9)
Atrial fibrillation or flutter — no. (%)	569 (24.7)	586 (25.2)	1155 (25.0)
Structural heart disease — no. (%) [†]	1330 (58.3)	1402 (60.9)	2732 (59.6)
Hypertension — no. (%)	1999 (86.9)	1996 (85.8)	3995 (86.3)
Coronary heart disease — no. (%)	668 (29.0)	737 (31.7)	1405 (30.4)
Valvular heart disease — no. (%)	379 (16.5)	380 (16.3)	759 (16.4)
Nonischemic cardiomyopathy — no. (%)	123 (5.3)	131 (5.6)	254 (5.5)
History of CHF, NYHA class II or III — no. (%)	464 (20.2)	515 (22.1)	979 (21.2)
LVEF — no. (%) [‡]			
<45%	255 (11.3)	285 (12.5)	540 (11.9)
<35%	92 (4.1)	87 (3.8)	179 (3.9)
Lone atrial fibrillation — no. (%) [§]	140 (6.1)	139 (6.0)	279 (6.0)
Pacemaker — no. (%)	214 (9.3)	243 (10.4)	457 (9.9)

ATHENA: Effect of Dronedarone on Cardiovascular Events in Atrial Fibrillation

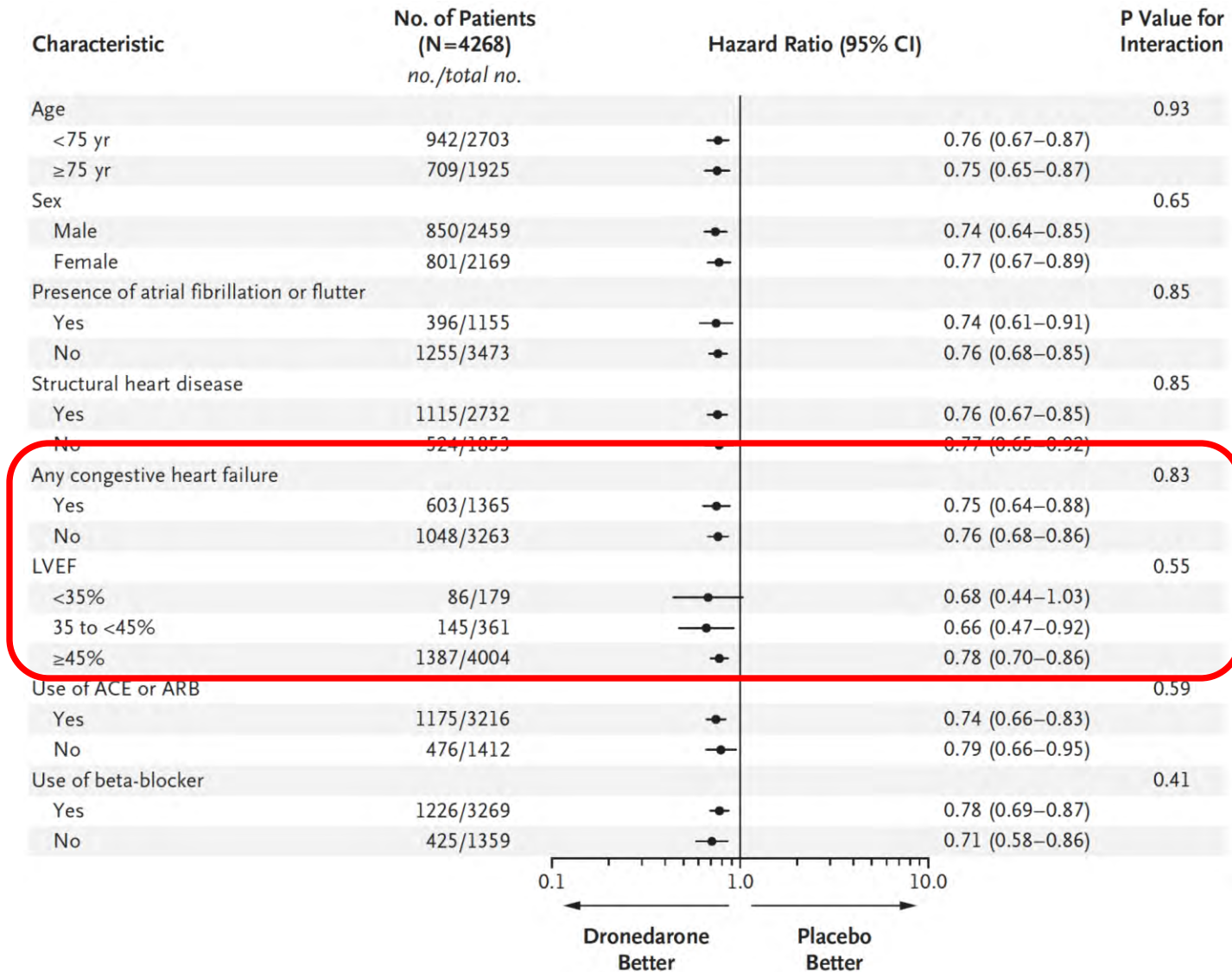
A Primary Outcome



No. at Risk

Placebo	2327	1858	1625	1072	385	3
Dronedarone	2301	1963	1776	1177	403	2

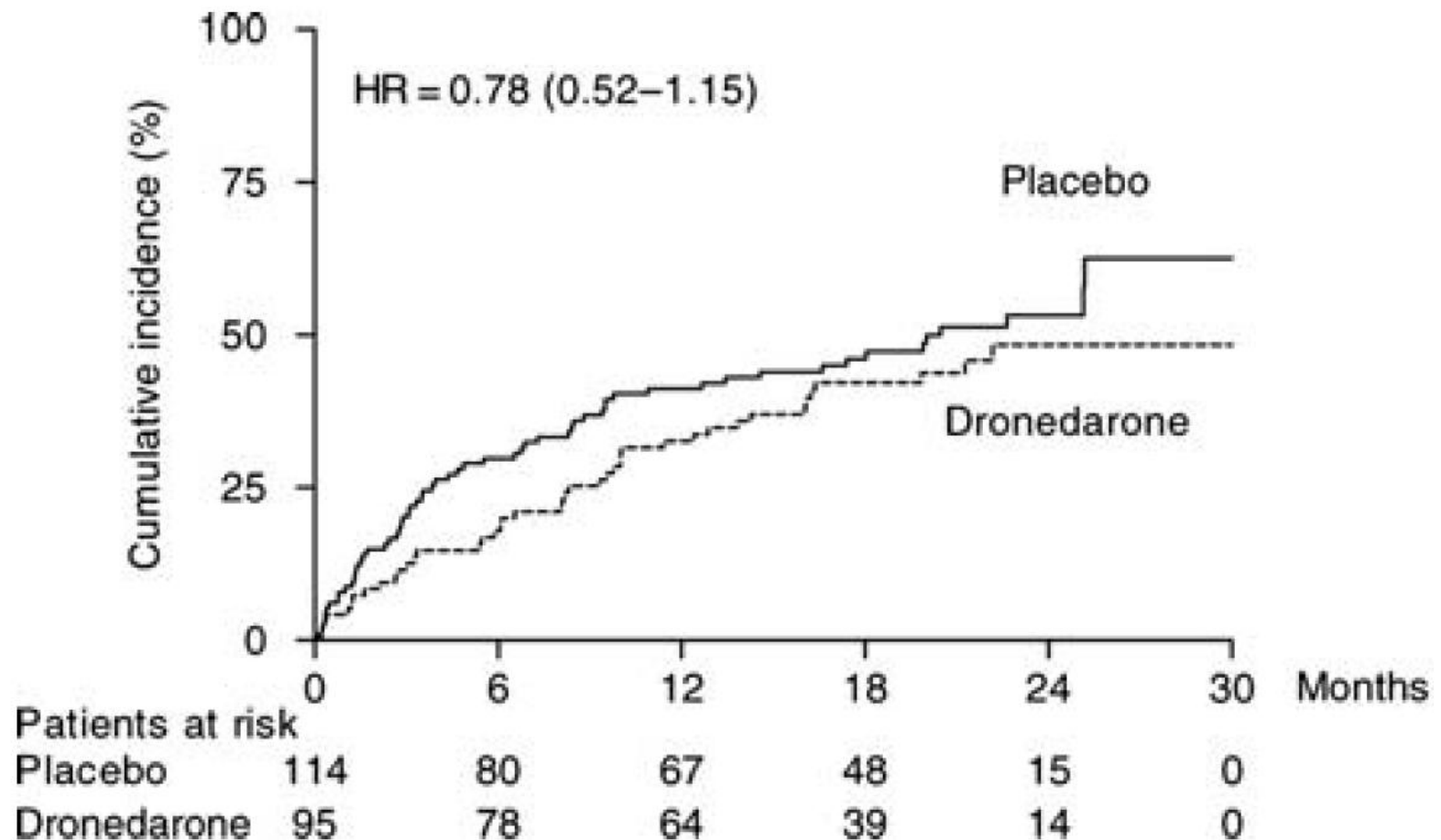
ATHENA: Effect of Dronedarone on Cardiovascular Events in Atrial Fibrillation



Dronedarone in patients with congestive heart failure: insights from **ATHENA**

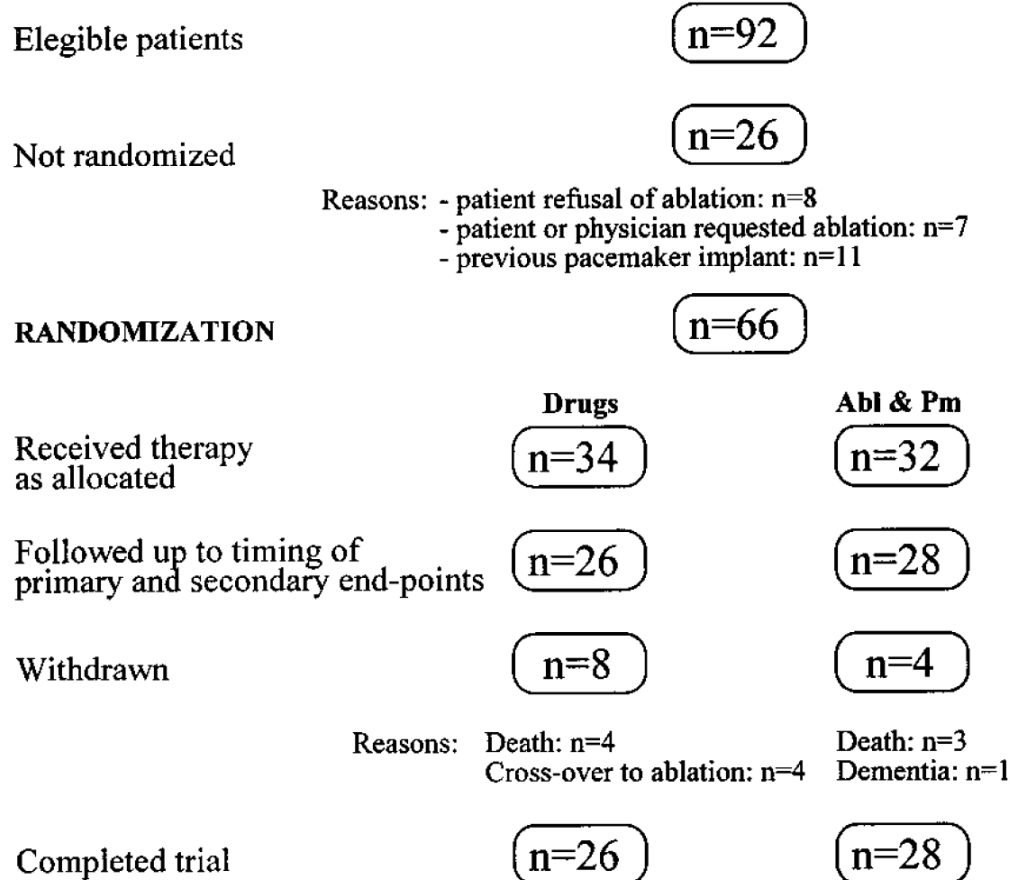
	NYHA II/III patients with LVEF ≤ 0.40 at baseline		Remaining patients	
	Placebo (n = 114)	Dronedarone (n = 95)	Placebo (n = 2167)	Dronedarone (n = 2168)
Age (years; SD)	72.0 (8.5)	71.3 (9.5)	71.7 (9.0)	71.6 (8.9)
Male gender (%)	81 (71.1%)	71 (74.7%)	1186 (54.7%)	1075 (49.6%)
Hypertension	86 (75.4%)	75 (78.9%)	1876 (86.6%)	1892 (87.3%)
Coronary heart disease	67 (58.8%)	51 (53.7%)	647 (29.9%)	600 (27.7%)
Ischaemic dilated cardiomyopathy	36 (31.6%)	35 (36.8%)	80 (3.7%)	57 (2.6%)
Non-rheumatic valvular heart disease	27 (23.7%)	28 (29.5%)	321 (14.8%)	300 (13.8%)
Non-ischaemic dilated cardiomyopathy	25 (21.9%)	18 (18.9%)	58 (2.7%)	62 (2.9%)
Pacemaker	23 (20.2%)	23 (24.2%)	215 (9.9%)	188 (8.7%)
Implanted cardioverter defibrillator	22 (19.3%)	19 (20.0%)	20 (0.9%)	23 (1.1%)

Dronedarone in Patients with Congestive Heart Failure: Insights from **ATHENA**



Assessment of Atrioventricular Junction Ablation and VVIR Pacemaker Versus Pharmacological Treatment in Heart Failure and Chronic AFib

Participant flow



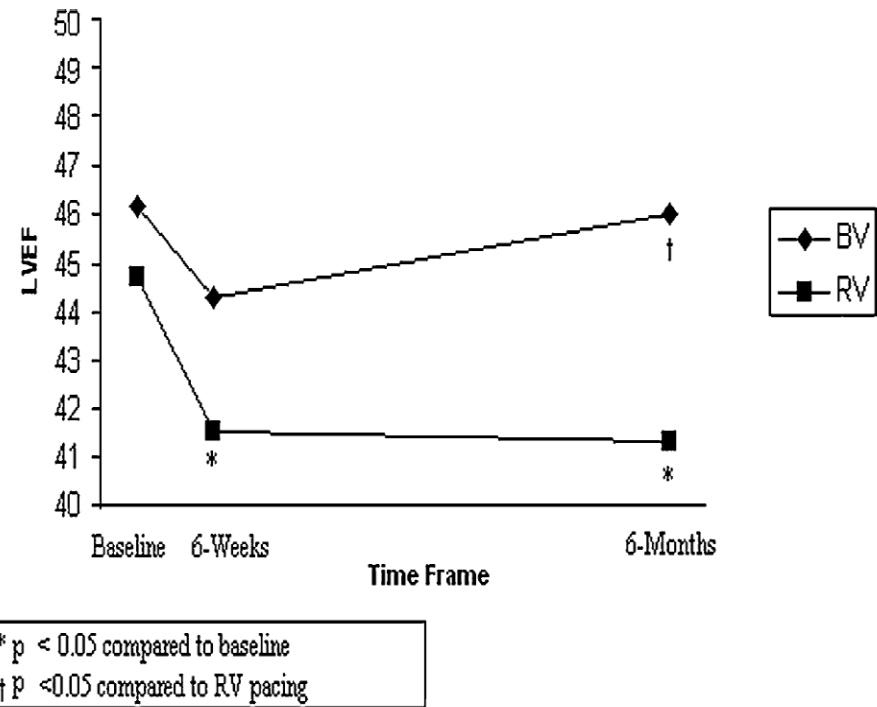
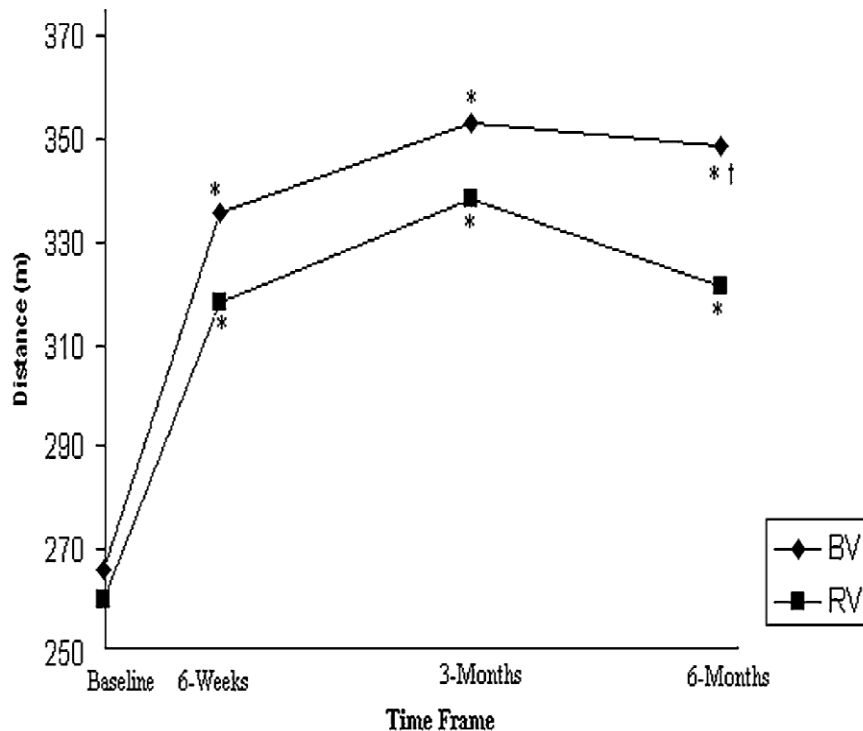
Assessment of Atrioventricular Junction Ablation and VVIR Pacemaker Versus Pharmacological Treatment in Heart Failure and Chronic AFib

								Difference, From Enrollment to Month 12				
	Enrollment			Month 12				Abl+Pm		Drugs		Abl+Pm vs Drugs, <i>P</i>
	Abl+Pm	Drugs	<i>P</i>	ABL+Pm	Drugs	<i>P</i>	% Reduction	%	<i>P</i>	%	<i>P</i>	
LHFQ questionnaire	43±19	44±15	0.83	32±20	37±18	0.34	−14	−26	0.02	−16	0.01	0.57
Specific Symptoms Scale												
Palpitations	5.5±2.7	5.7±2.6	0.78	1.0±1.4	4.5±2.9	0.000	−78	−82	0.000	−21	0.05	0.000
Effort dyspnea	6.8±2.7	6.3±2.3	0.47	4.5±2.4	5.8±2.2	0.04	−22	−34	0.000	−8	0.38	0.01
Rest dyspnea	3.5±2.7	3.0±3.0	0.52	1.6±2.8	1.5±2.3	0.89	+11	−54	0.003	−50	0.05	0.66
Exercise intolerance	6.5±2.6	5.8±2.0	0.27	4.4±2.7	5.5±2.0	0.10	−20	−32	0.000	−5	0.55	0.005
Easy fatigue	4.1±2.9	2.8±2.8	0.10	3.4±3.2	4.1±2.8	0.40	−17	−17	0.20	+46	0.05	0.02
Chest discomfort	0.9±2.1	0.6±1.6	0.56	0.4±1.9	0.8±2.2	0.48	−50	−56	0.04	+33	0.28	0.02
NYHA class	2.8±0.7	2.7±0.6	0.58	2.4±0.5	2.5±0.8	0.58	−4	−14	0.006	−7	0.17	0.30
Activity Scale	2.7±0.8	2.8±0.7	0.63	2.3±0.8	2.6±0.9	0.20	−12	−15	0.02	−7	0.10	0.35

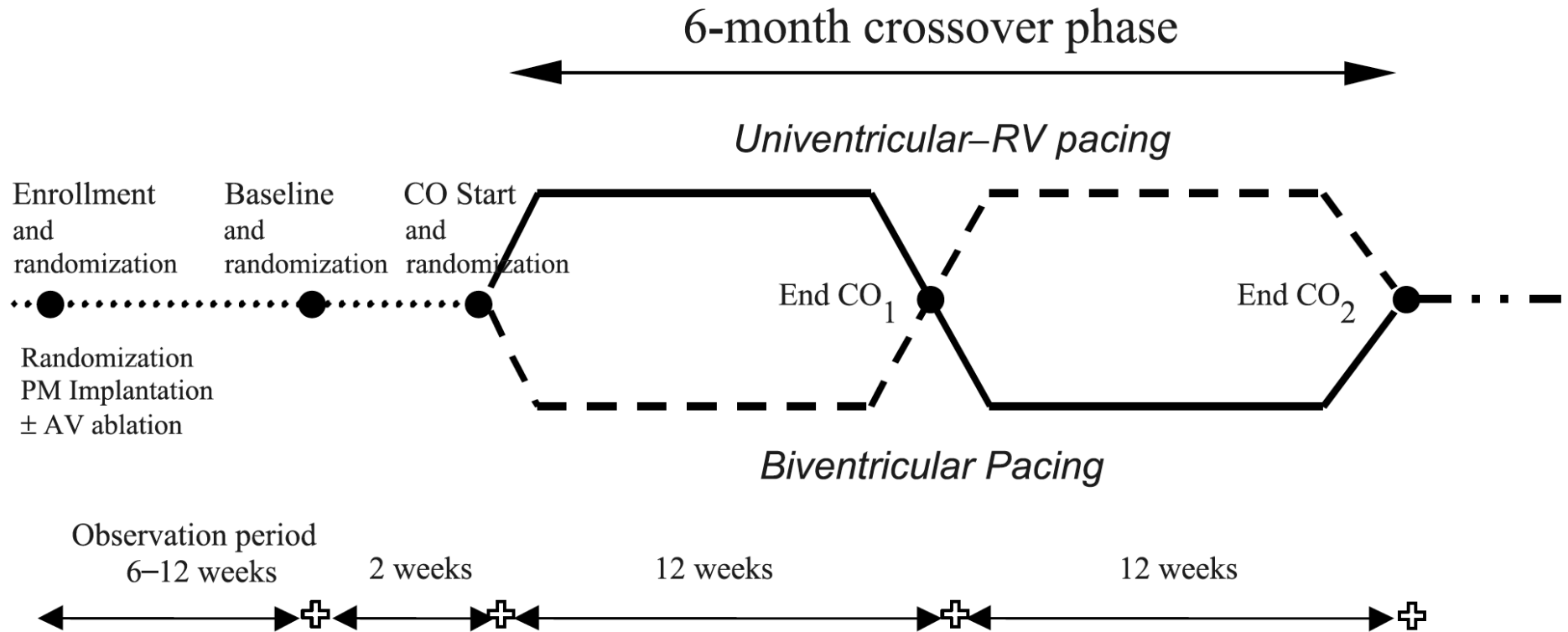
Assessment of Atrioventricular Junction Ablation and VVIR Pacemaker Versus Pharmacological Treatment in Heart Failure and Chronic AFib

Event	Abl + Pm (n=32)	Drugs (n=34)	<i>P</i>
Death			
Total	3 (9)	4 (12)	0.53
Cardiac, sudden	1 (3)	4 (12)	0.20
Cardiac, nonsudden	1 (3)	0 (0)	0.48
Hospitalization	9 (28)	13 (38)	0.27
Episodes of acute pulmonary edema	0 (0)	3 (9)	0.13
Episodes of congestive heart failure	13 (41)	15 (44)	0.48
Stroke	0 (0)	1 (3)	0.13

Left Ventricular-Based Cardiac Stimulation Post AV Nodal Ablation Evaluation (The PAVE Study): Results on 6MW and EF



Biventricular and right-univentricular pacing in heart failure patients with chronic Afib: Multisite STimulation In Cardiomyopathy (MUSTIC) Study



Biventricular and right-univentricular pacing in heart failure patients with chronic atrial fibrillation

	Baseline	All patients	Distribution in the two treatment-arms		<i>P</i> value
			1st treatment arm (BIV-UniRV)	2nd treatment arm (UniRV-Biv)	
Number of patients	45	43	25	18	
Sex ratio men/women	37/8	35/8	21/4	14/4	0.70
Age (years)	66 ± 9	65 ± 8	65 ± 9	66 ± 9	0.76
Weight (kg)	79 ± 17	76 ± 14	77 ± 13	74 ± 14	0.70
6-min walked distance (m)	324 ± 76	329 ± 85	338 ± 95	317 ± 71	0.64
Peak VO ₂ (ml . min ⁻¹ kg ⁻¹)	12.7 ± 3.8	12.9 ± 4.8	12.8 ± 4.9	13 ± 4.8	0.9
Quality-of-life score	46 ± 22	44 ± 22	40 ± 23	50 ± 20	0.11
Heart rate (beats . min ⁻¹)	73 ± 6	74 ± 5	75 ± 6	74 ± 5	0.53
Paced QRS duration (ms)	207 ± 17	209 ± 18	209 ± 21	208 ± 12	0.71
His bundle ablation (Yes/No)	29/16	27/16	18/6	9/9	0.14
Previous PM (Yes/No)	23/22	22/21	13/12	9/9	0.90
Left ventricular EF (%)	25 ± 10	26 ± 10	23 ± 7	30 ± 12	0.07
Left ventricular EDD (mm)	68 ± 7	68 ± 8	70 ± 9	66 ± 7	0.07

Biventricular and right-univentricular pacing in heart failure patients with Afib: Results of the ITT analysis

		Right uni ventricular		Biventricular		Δ	<i>P</i>
		n	mean $\pm$ SD	n	mean $\pm$ SD		
Treatment arm 1	6 min walked test distance (m)	18	360 $\pm$ 101	18	389 $\pm$ 109	+29	
	Peak VO ₂ (ml . kg ⁻¹ min ⁻¹)	17	13.9 $\pm$ 4.4	17	15.7 $\pm$ 4.1	+1.8	
	QOL score	21	35.9 $\pm$ 20.1	21	32.4 $\pm$ 21.8	-3.5	
Treatment arm 2	6 min walked test distance (m)	20	324.2 $\pm$ 98	20	332.5 $\pm$ 128.1	+8	
	Peak VO ₂ (ml . kg ⁻¹ min ⁻¹)	15	12.8 $\pm$ 3.6	15	13.7 $\pm$ 3.9	+0.9	
	QOL score	18	41.5 $\pm$ 23.1	18	36.0 $\pm$ 19.5	-5.5	
Treatment arms 1+2	6 min walked test distance (m)	38	341 $\pm$ 100	38	359 $\pm$ 121	+18	ns
	Peak VO ₂ (ml . kg ⁻¹ min ⁻¹)	32	13.4 $\pm$ 4.0	32	14.8 $\pm$ 4.1	+1.4	0.08
	QOL score	39	38.5 $\pm$ 21.4	39	34.1 $\pm$ 20.6	-4.4	ns
	Patient preference	39*	4	39	33		0.001

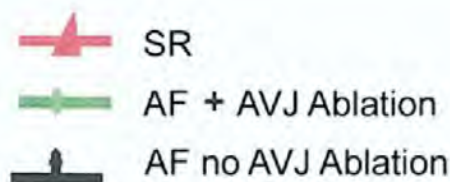
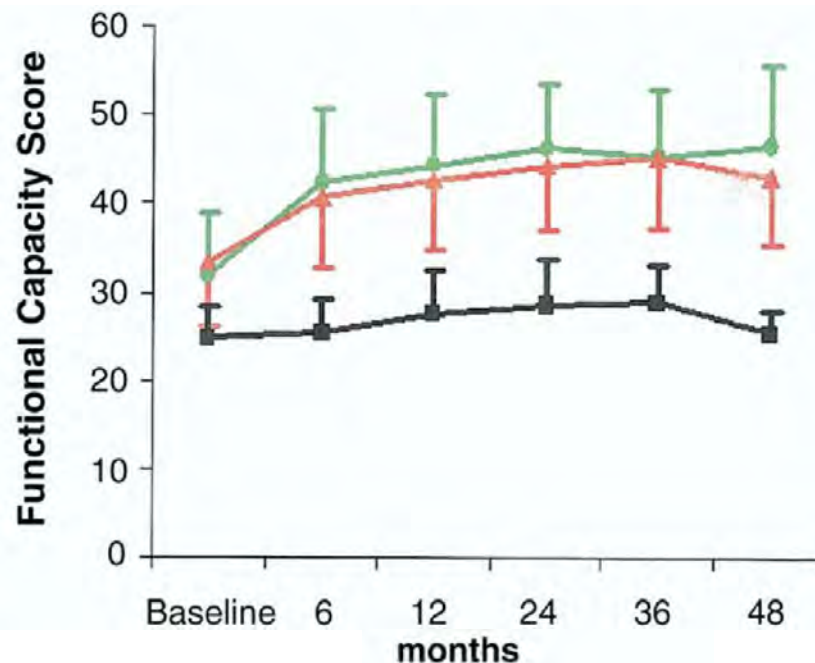
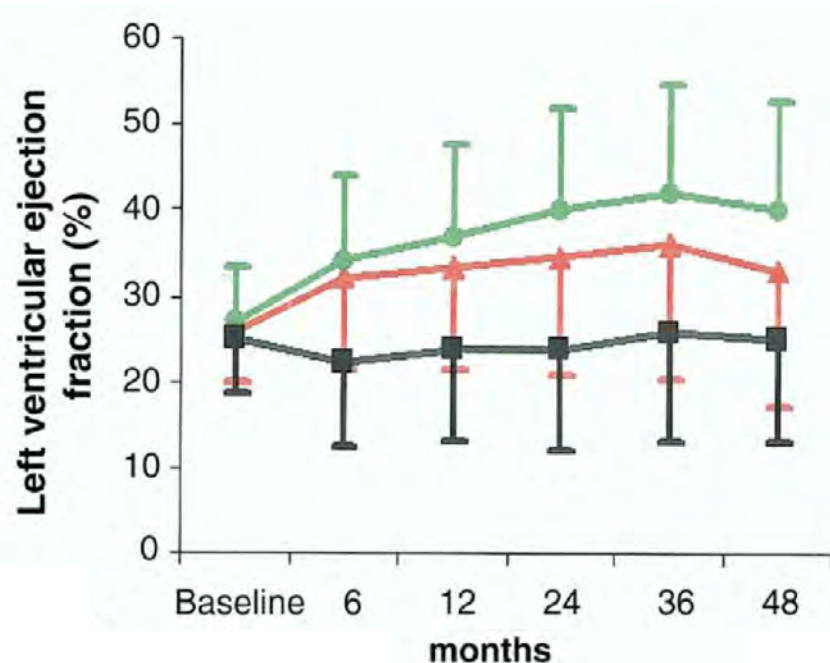
Long-Term Benefits of Biventricular Pacing in Congestive Heart Failure: Results From MUSTIC

Pacing Mode	SR Group		AF Group	
	VVI40	BiV	RV-VVIR 70	BiV
Hospitalization (no.)	22	11	28	9
Total time spent in pacing mode (no. of months)	156	475	198	218
Hospitalization per month	0.14	0.02	0.14	0.04

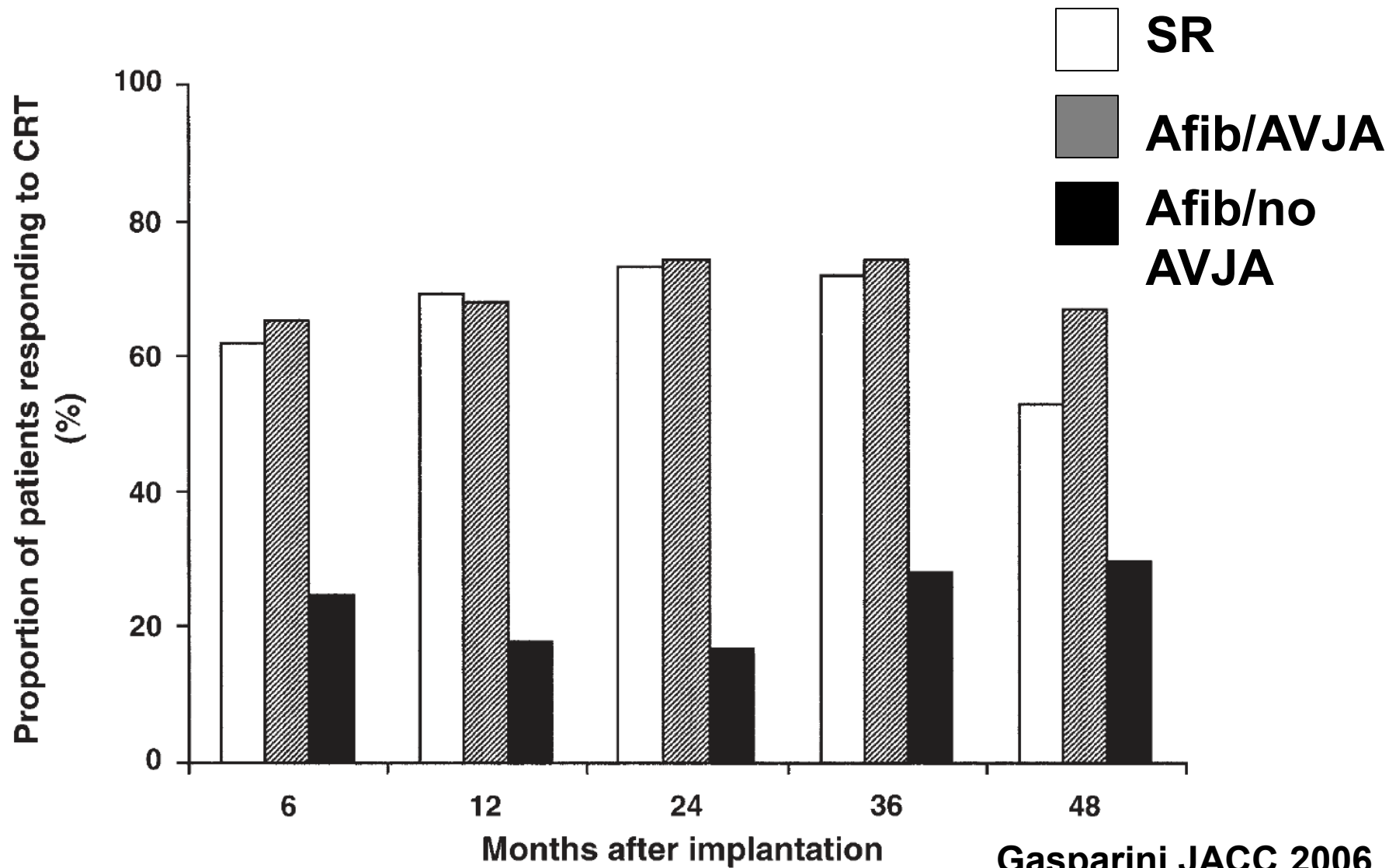
Four-Year Efficacy of CRT on Exercise Tolerance and Disease Progression: The Importance of Performing AVJ Ablation in Patients With AFib

	SR (n = 511)	AF (n = 162)	p Value
Follow-up (months)*	26.1 (12.4–42.2)	24.6 (12.7–42.2)	0.562
Age (yrs)†	63.4 (10.0)	66.0 (8.3)	0.002
Male gender (%)†	395 (77.3)	139 (85.8)	0.019
Functional NYHA functional class III–IV (%)‡	452 (89.7)	154 (96.9)	0.003
QRS duration (ms)†	165.3 (29.5)	165.0 (35.5)	0.915
Coronary artery disease (%)‡	241 (47.2)	60 (37.1)	0.029
LVEF (%)†	26.0 (7.0)	26.3 (6.7)	0.647
LVEDD (mm)†	67.0 (9.0)	66.0 (8.8)	0.259
LVESV (ml)†	196 (53)	186 (45)	0.062
Peak oxygen consumption (ml/min/kg)†	13.1 (2.8)	12.1 (2.2)	0.005
6-min walking distance (m)†	332 (117)	311 (107)	0.122
Functional capacity score†	33.4 (7.3)	29.6 (6.5)	0.014
CRT with a defibrillator (%)‡	299 (58.5)	79 (48.8)	0.036
Beta-blockers (%)‡	424 (83.1)	135 (83.3)	1.000
ACE inhibitors (%)‡	460 (90.4)	152 (93.8)	0.204
Antialdosteronic agents (%)‡	267 (52.5)	85 (52.5)	1.000
Diuretics (%)‡	449 (88.2)	148 (91.4)	0.314
Negative chronotropic drugs (%)‡	435 (85.1)	160 (98.7)	<0.0001
Lead position: lateral or posterolateral region (%)‡	454 (89)	142 (88)	0.885

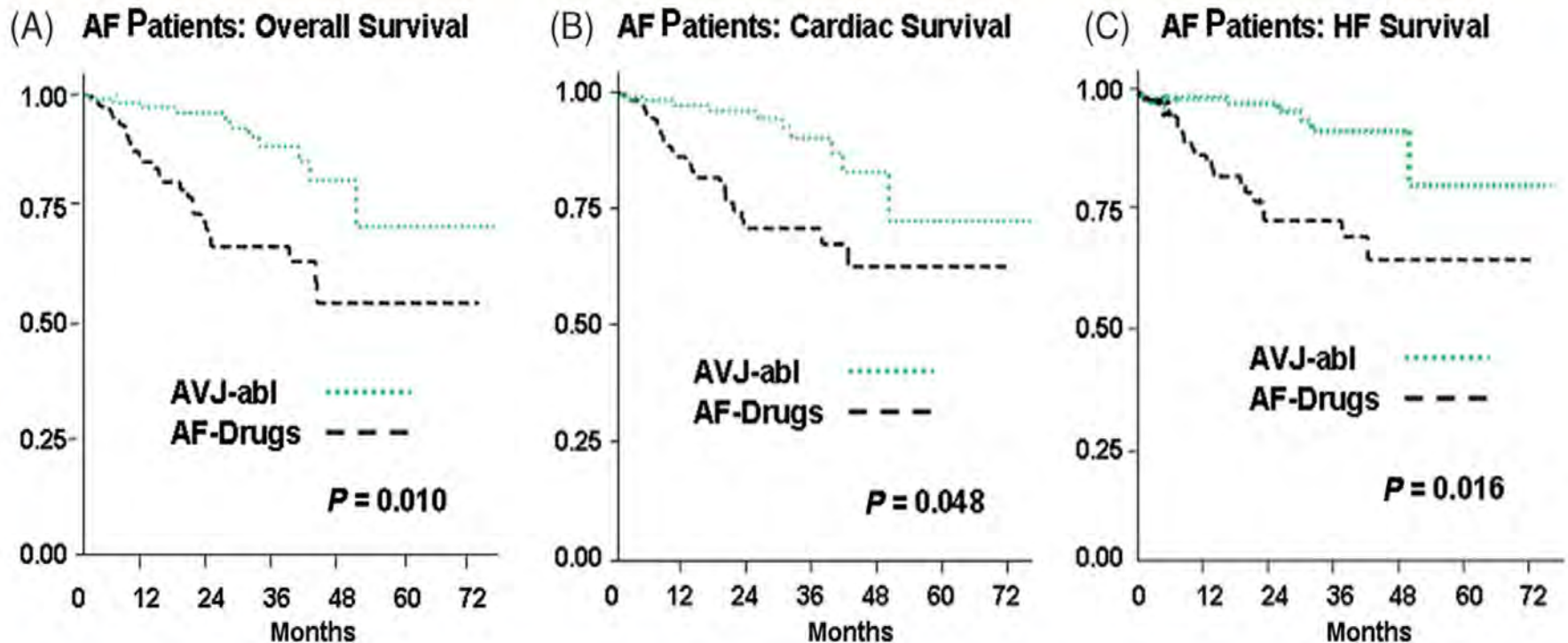
Four-Year Efficacy of CRT on Exercise Tolerance and Disease Progression: The Importance of Performing AVJ Ablation in Patients With AFib



Percentage of responders to CRT in AFib: The Importance of Performing AVJ Ablation

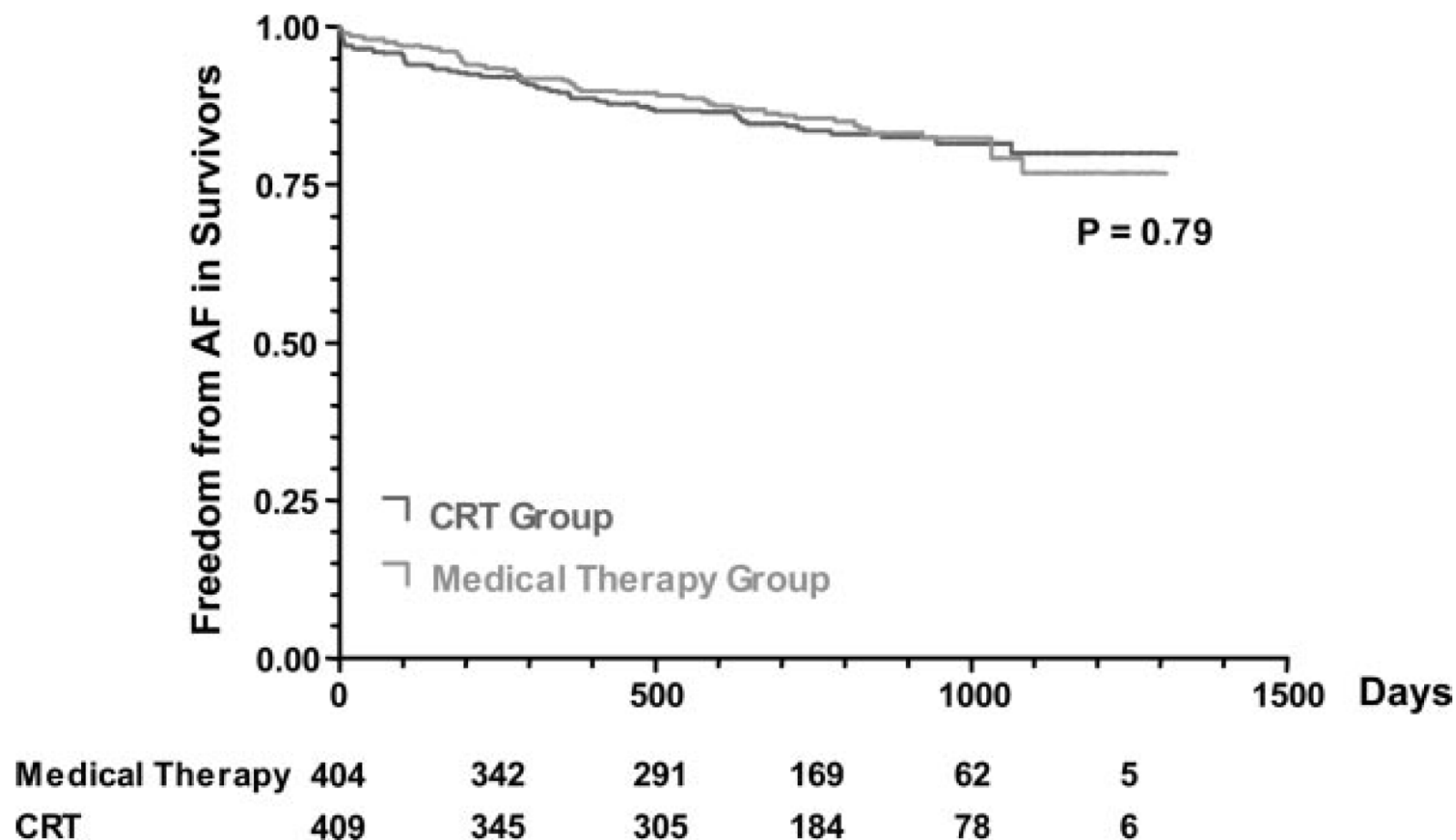


Long-term Survival in Patients Undergoing CRT: The Importance of **Atrio-Ventricular Junction Ablation** in Patients with Permanent AFib



AVJ ablation patients suspended both digoxin and amiodarone

Effect of CRT on the Incidence of Afib in Patients With Severe Heart Failure: Results from CARE-HF

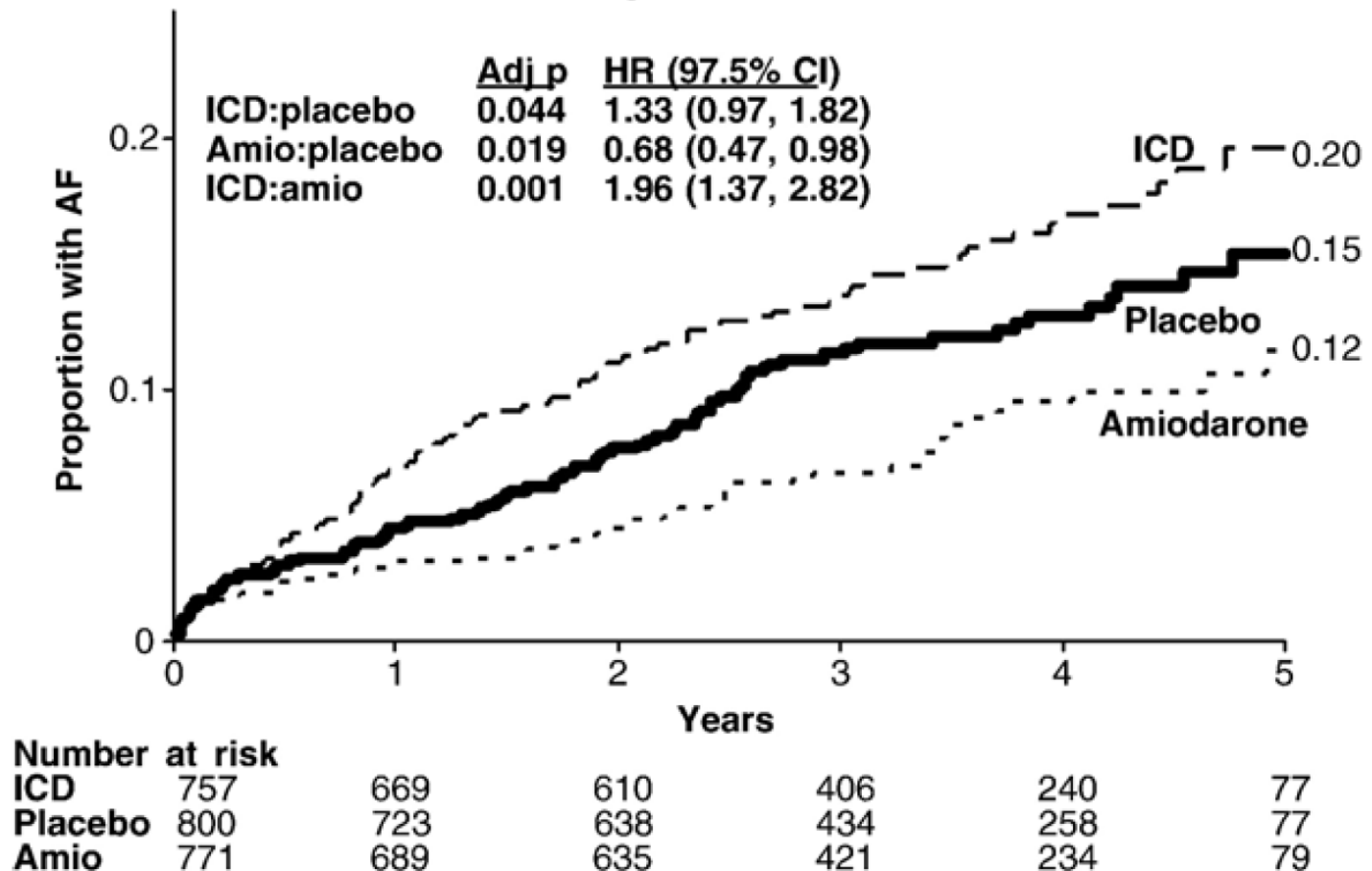


Role of **Amiodarone** vs **ICD** in Patients with Afib and and Heart Failure

Characteristic	SR (n = 2328)	AF (n = 173)	P*
Randomized treatment			.049
ICD	33% (757)	38% (65)	
Amiodarone	33% (771)	37% (64)	
Placebo	34% (800)	25% (44)	
Age	60 (51, 68)	67 (60, 74)	.001
Female	24% (566)	9% (16)	.001
Weight (lb)	189 (163, 218)	202 (168, 236)	.002
NYHA class			.004
II	71% (1646)	60% (104)	
III	29% (682)	40% (69)	
Ejection fraction	25 (20, 30)	24 (20, 30)	.36
Heart rate (beat/min)	73 (64, 84)	74 (64, 85)	.85
Medications			
β -Blocker	69% (1610)	68% (117)	.67
ACE inhibitor	85% (1976)	83% (143)	.44
Spironolactone	19% (447)	20% (35)	.74
Statin	39% (919)	23% (40)	.001
Warfarin	30% (690)	92% (160)	.001

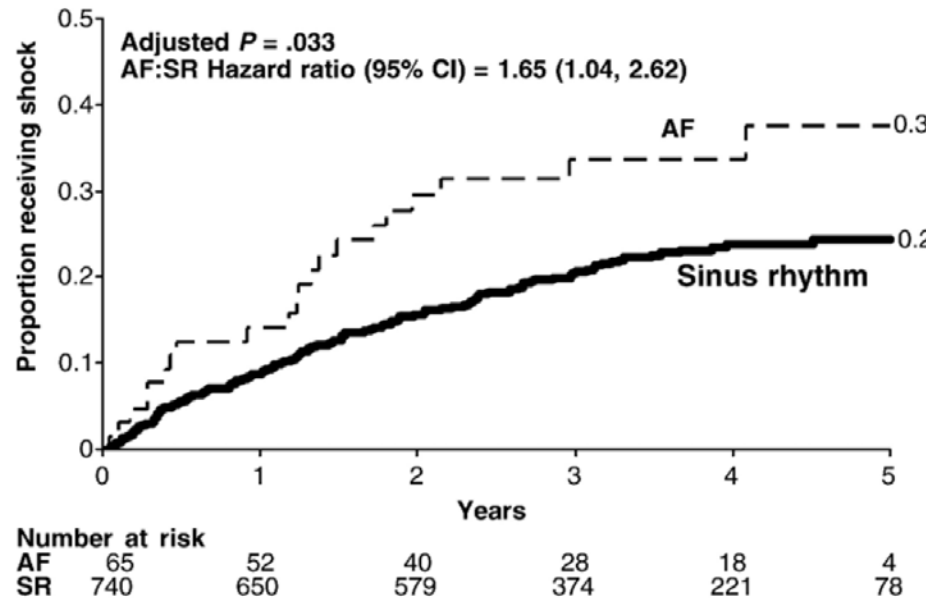
Role of Amiodarone or ICD in Patients with AFib and Heart Failure

AF reported in patients with
sinus rhythm at baseline

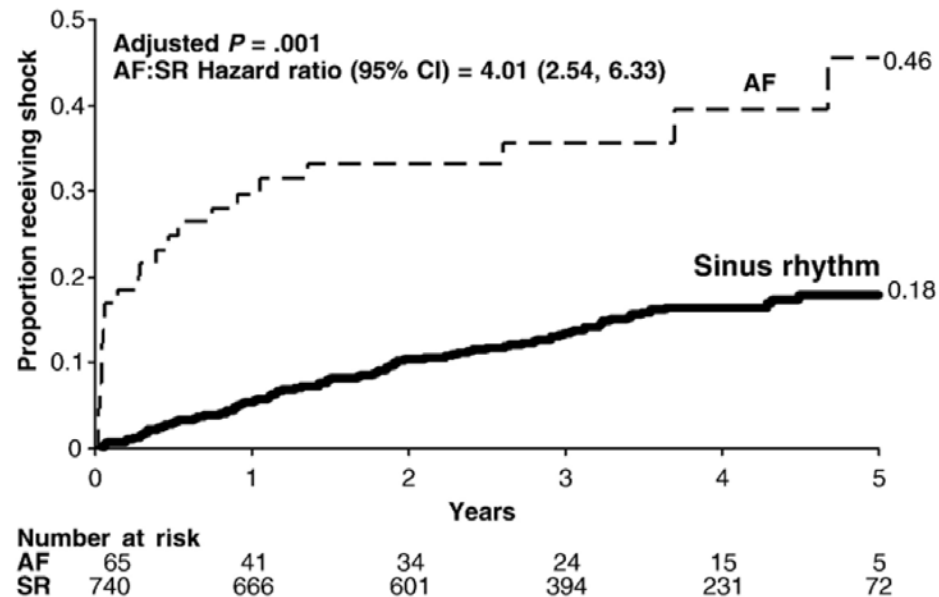


Role of Amiodarone or ICD in Patients with Afib and Heart Failure: Incidence of **Appropriate** or **Inappropriate** Shocks

Appropriate Shock



Inappropriate Shock





2010 Focused Update of ESC guidelines on device therapy in heart failure

Recommendations in patients with heart failure and permanent atrial fibrillation

Recommendations	Patient population	Class ^a	Level ^b	Ref. ^c
CRT-P/CRT-D ^d should be considered to reduce morbidity	NYHA function class III/IV LVEF $\leq 35\%$, QRS ≥ 130 ms Pacemaker dependency induced by AV nodal ablation	Ia	B	27–40
CRT-P/CRT-D ^d should be considered to reduce morbidity	NYHA function class III/IV LVEF $\leq 35\%$, QRS ≥ 130 ms Slow ventricular rate and frequent pacing ^e	Ia	C	—

AFFIRM – Rate Control vs Rhythm Control in AFib

HR < 80 bpm at rest and < 110 bpm 6MW

CHARACTERISTIC	OVERALL (N=4060)	RATE-CONTROL GROUP (N=2027)	RHYTHM-CONTROL GROUP (N=2033)	P VALUE
Age — yr	69.7±9.0	69.8±8.9	69.7±9.0	0.82
Female sex — no. (%)	1594 (39.3)	823 (40.6)	771 (37.9)	0.08
Ethnic minority group — no. (%)	461 (11.4)	241 (11.9)	220 (10.8)	0.28
Predominant cardiac diagnosis — no. (%)				0.29
Coronary artery disease	1059 (26.1)	497 (24.5)	562 (27.6)	
Cardiomyopathy	194 (4.8)	99 (4.9)	95 (4.7)	
Hypertension	2063 (50.8)	1045 (51.6)	1018 (50.1)	
Valvular disease	198 (4.9)	98 (4.8)	100 (4.9)	
Other	42 (1.0)	23 (1.1)	19 (0.9)	
No apparent heart disease	504 (12.4)	265 (13.1)	239 (11.8)	
History of congestive heart failure — no. (%)	939 (23.1)	475 (23.4)	464 (22.8)	0.64
Duration of qualifying atrial fibrillation ≥2 days — no. (%)	2808 (69.2)	1406 (69.4)	1402 (69.0)	0.80
First episode of atrial fibrillation (vs. recurrent episode) — no. (%)†	1391 (35.5)	700 (35.8)	691 (35.3)	0.74
Any prerandomization failure of an antiarrhythmic drug — no. (%)	713 (17.6)	364 (18.0)	349 (17.2)	0.51
Size of left atrium normal — no. (%)‡	1103 (35.3)	549 (35.3)	554 (35.3)	0.98
Left ventricular ejection fraction — %§	54.7±13.5	54.9±13.1	54.6±13.8	0.74
Normal left ventricular ejection fraction — no. (%)‡	2244 (74.0)	1131 (74.9)	1113 (73.2)	0.29

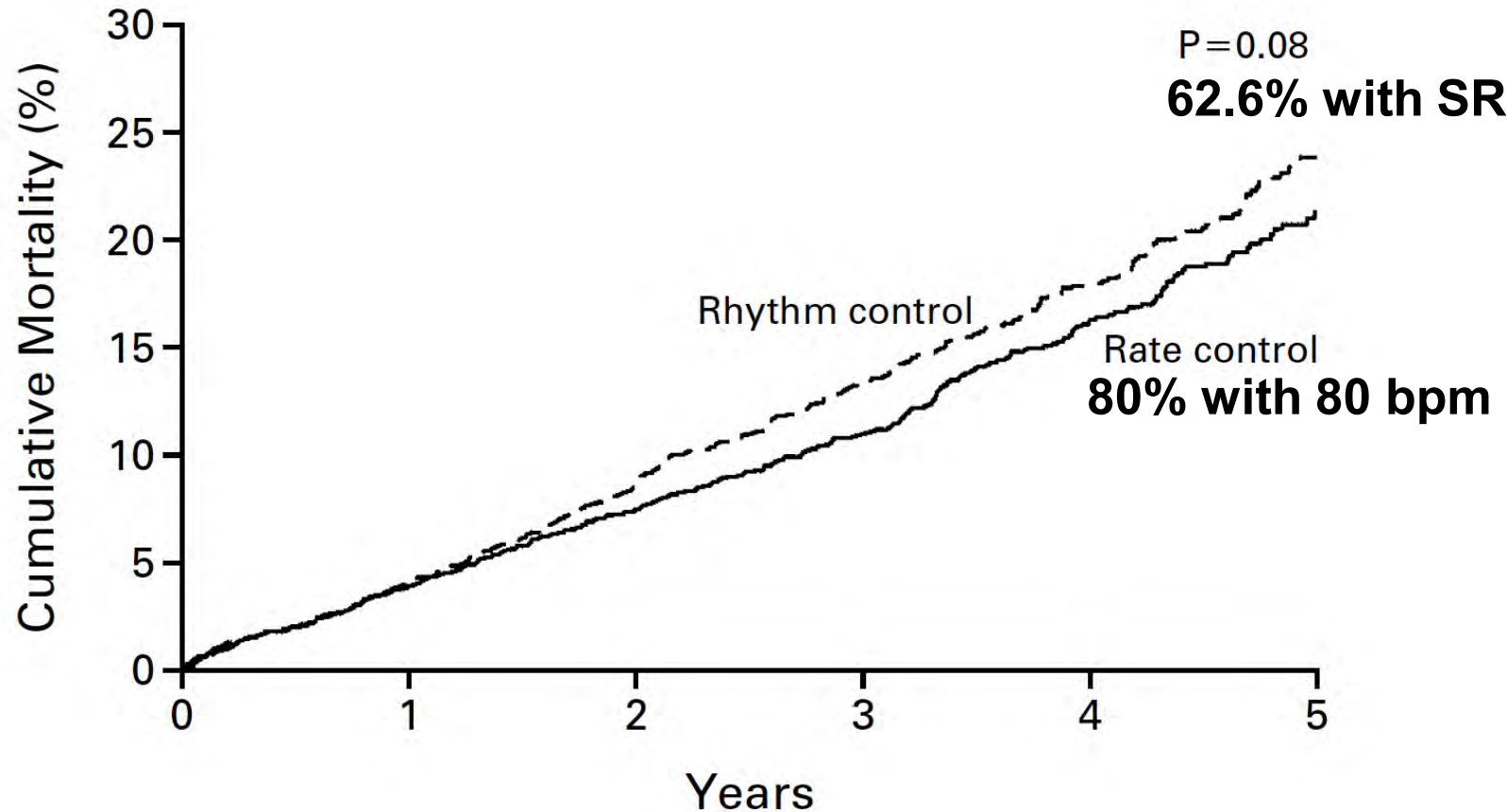
AFFIRM – Drugs Used in the resp. Study Groups

DRUG	RATE-CONTROL GROUP		RHYTHM-CONTROL GROUP	
	USED DRUG FOR INITIAL THERAPY	USED DRUG AT ANY TIME	USED DRUG FOR INITIAL THERAPY	USED DRUG AT ANY TIME
	no. of patients (%)			
Rate control				
Data available	1957	2027	1266	2033
Digoxin	949 (48.5)	1432 (70.6)	417 (32.9)	1106 (54.4)
Beta-blocker	915 (46.8)	1380 (68.1)	276 (21.8)	1008 (49.6)
Diltiazem	583 (29.8)	935 (46.1)	198 (15.6)	610 (30.0)
Verapamil	187 (9.6)	340 (16.8)	56 (4.4)	204 (10.0)
Rhythm control				
Data available	1265	2027	1960	2033
Amiodarone	2 (0.2)†	207 (10.2)	735 (37.5)	1277 (62.8)
Sotalol	1 (0.1)†	84 (4.1)	612 (31.2)	841 (41.4)
Propafenone	2 (0.2)†	45 (2.2)	183 (9.3)	294 (14.5)
Procainamide	0	30 (1.5)	103 (5.3)	173 (8.5)
Quinidine	2 (0.2)†	14 (0.7)	92 (4.7)	151 (7.4)
Flecainide	0	29 (1.4)	88 (4.5)	169 (8.3)
Disopyramide	0	7 (0.3)	42 (2.1)	87 (4.3)
Moricizine	0	2 (0.1)	14 (0.7)	35 (1.7)
Dofetilide	0	5 (0.2)	0	13 (0.6)

EC in 368 patients

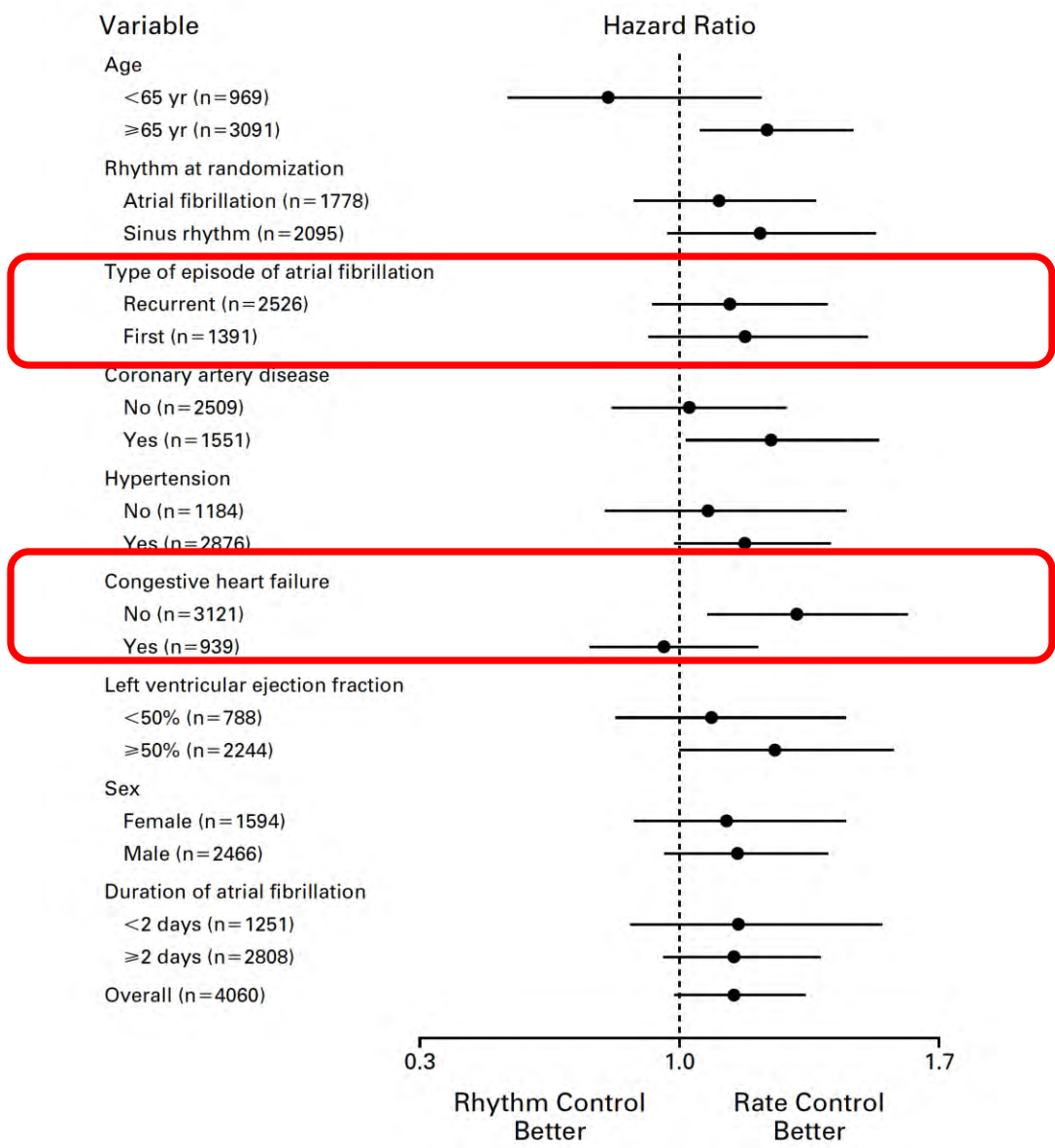
AFFIRM NEJM 2002

AFFIRM – Cumulative Mortality

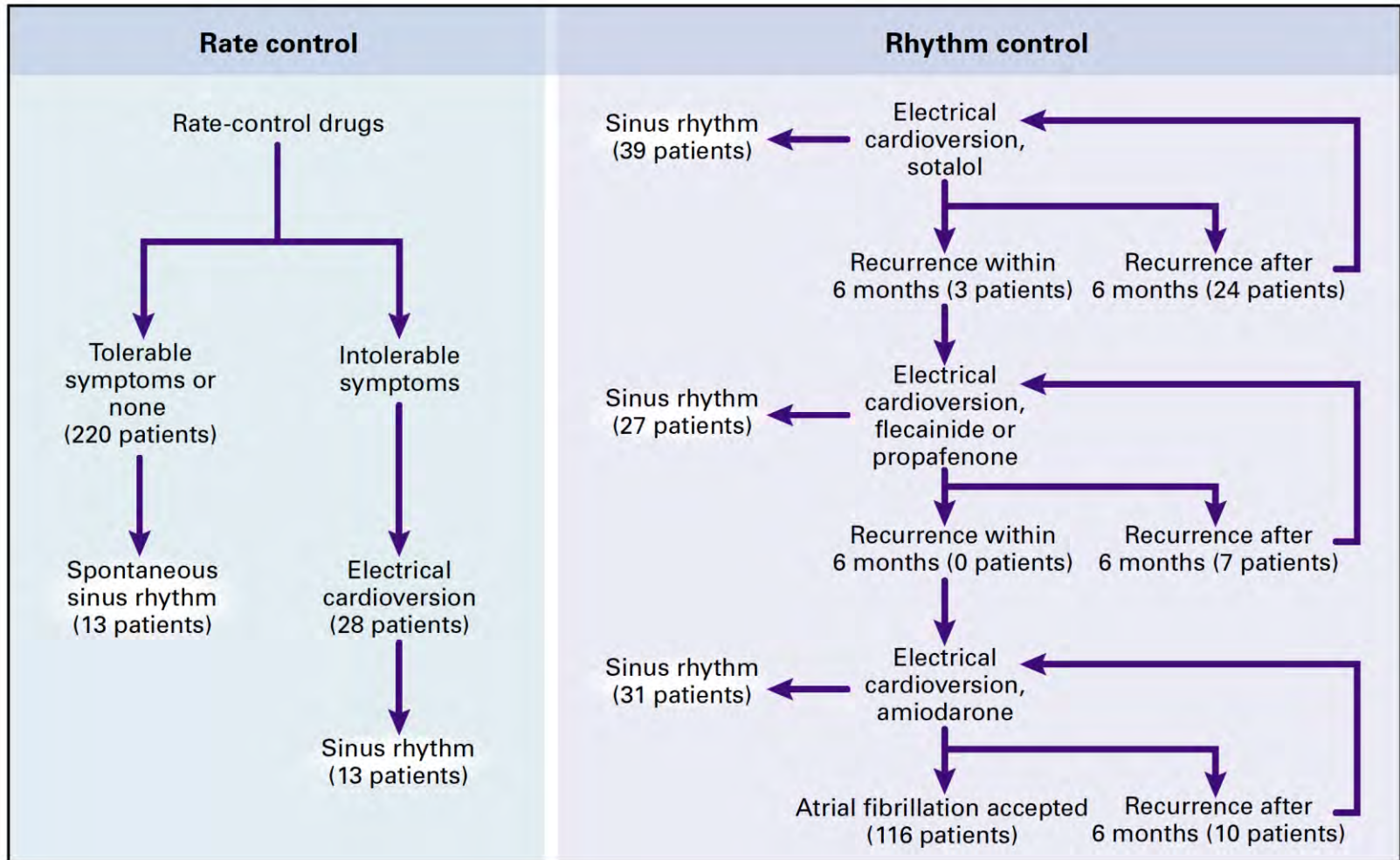


No. OF DEATHS		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

Hazard Ratios for Death in Prespecified Subgroups



A Comparison of Rate Control vs Rhythm Control in Patients with Recurrent **Persistent** Afib



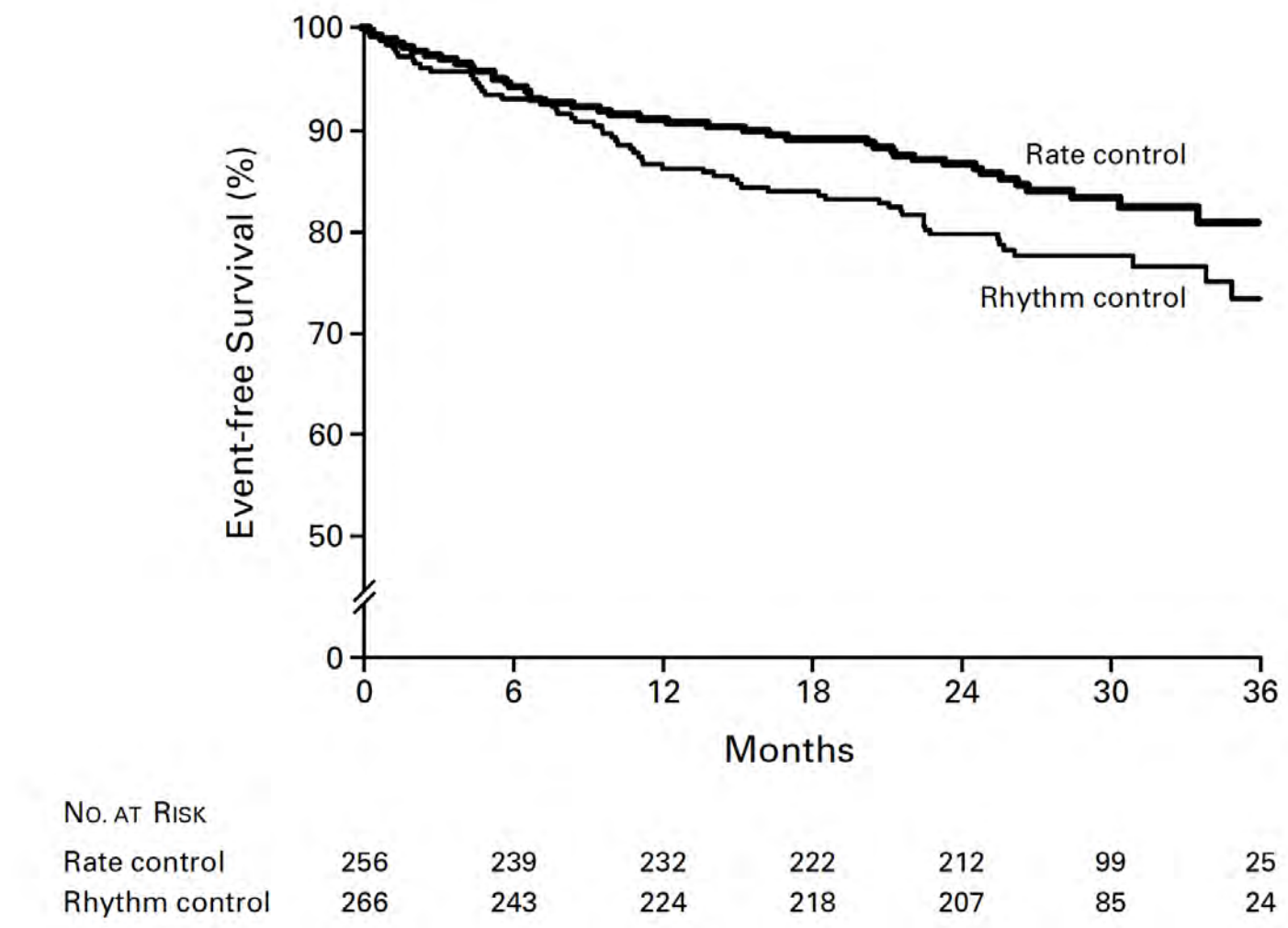
**26 patients (10%) had SR
at the end of the study**

**103 patients (39%) had SR
Median of 2 electrical cardioversion**

A Comparison of Rate Control vs Rhythm Control in Patients with Recurrent **Persistent** Afib

CHARACTERISTIC	RATE CONTROL (N=256)	RHYTHM CONTROL (N=266)
Age — yr	68±9	68±8
Male sex — no. (% of patients)	161 (63)	170 (64)
Atrial fibrillation — % of patients	93	93
Atrial flutter — % of patients	7	7
Duration of atrial fibrillation — days		
Median	337	309
Range	14–4820	10–14,399
Duration of current episode of atrial fibrillation — days		
Median	32	34
Range	1–399	1–395
Coronary artery disease — % of patients	29	26
Old myocardial infarction — % of patients	16	14
History of heart failure — % of patients	51	49
History of cerebrovascular accident — % of patients	16	12
NYHA class — % of patients†		
I	49	51
II	48	46
III	3	3

A Comparison of Rate Control vs Rhythm Control in Patients with Recurrent **Persistent** Afib



Rhythm Control versus Rate Control for Atrial Fibrillation and Heart Failure

Table 1. Baseline Characteristics of the Patients.*

Variable	Rhythm-Control Group (N=682)	Rate-Control Group (N=694)
Male sex (%)	78	85
Age (yr)	66±11	67±11
Body-mass index†	27.8±5.4	28.0±5.1
Nonwhite race (%)‡	16	13
NYHA class III or IV (%)		
At baseline	32	31
During previous 6 mo	76	76
Predominant cardiac diagnosis (%)§		
Coronary artery disease	48	48
Valvular heart disease	5	5
Nonischemic cardiomyopathy	36	39
Congenital heart disease	1	1
Hypertensive heart disease	10	7
Coexisting conditions (%)		
Hypertension	49	46
Diabetes	22	20
Previous stroke or transient ischemic attack	11	8
Left ventricular ejection fraction (%)	27±6	27±6
Primary classification of atrial fibrillation (%)		
Paroxysmal	33	30
Persistent¶	67	70
≥6 Mo since first diagnosis of atrial fibrillation (%)	41	46
Atrial fibrillation on electrocardiography (%)	54	61

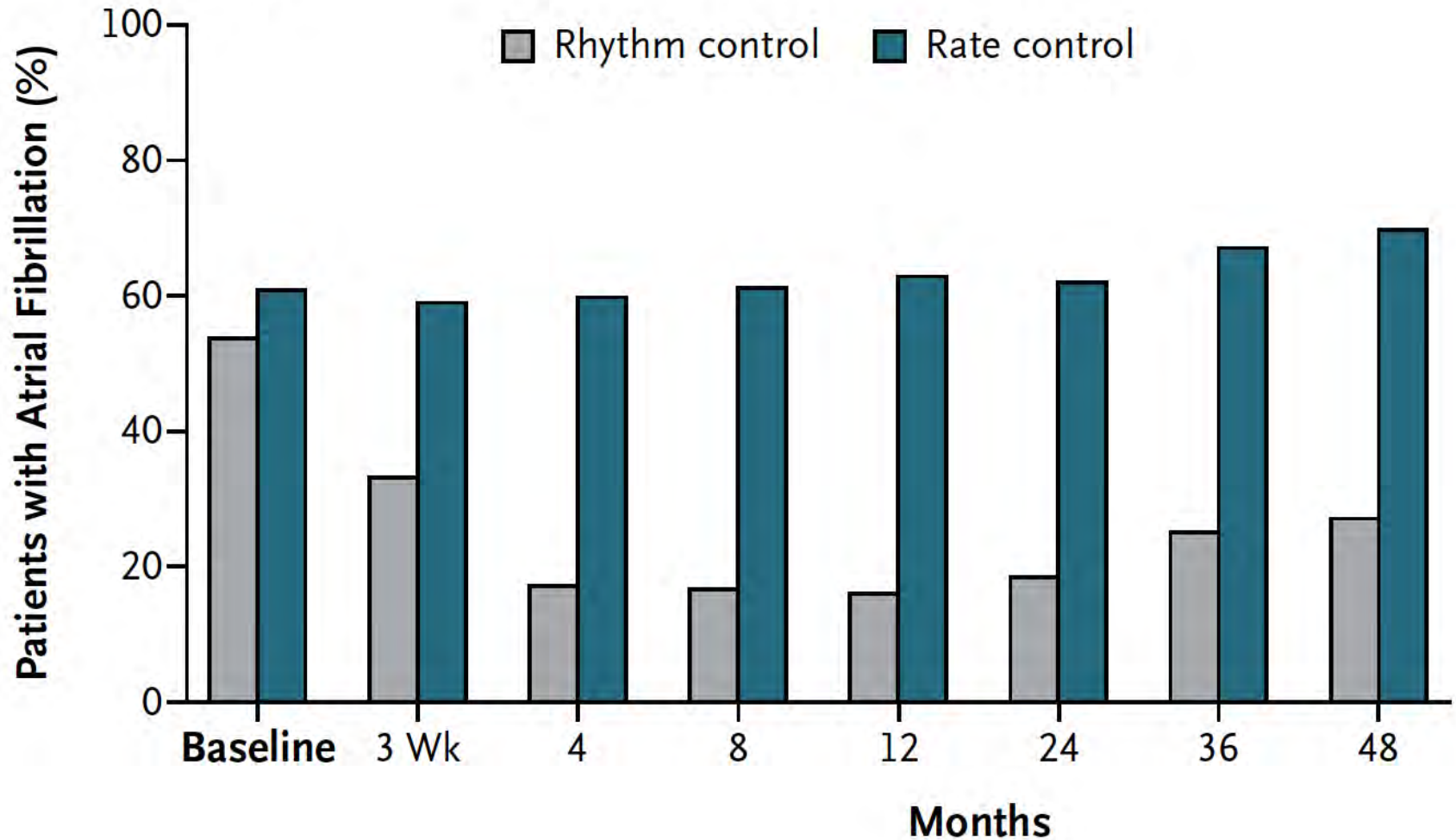
Rhythm Control versus Rate Control for Atrial Fibrillation and Heart Failure

Table 2. Medical Therapy at 12 Months.*

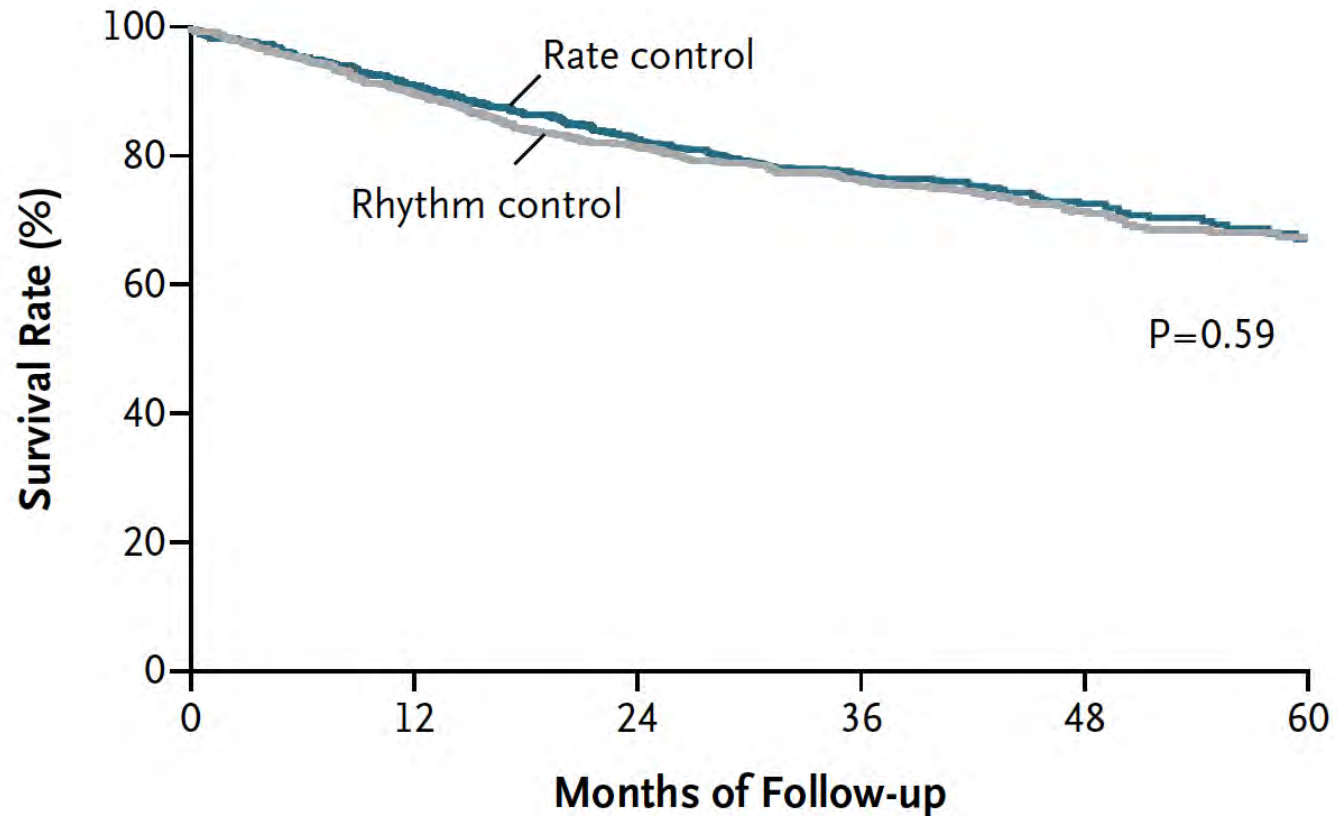
Drug	Rhythm-Control Group (N = 682)	Rate-Control Group (N = 694)	P Value
	<i>percent</i>		
Amiodarone	82	7	<0.001
Sotalol	2	<1	0.02
Dofetilide	<1	<1	0.62
Beta-blocker	80	88	<0.001
Digoxin	51	75	<0.001
Verapamil or diltiazem	2	3	0.10
ACE inhibitor	81	82	0.41
ARB	16	13	0.09
ACE inhibitor or ARB	94	94	0.57
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

Rhythm Control versus Rate Control for Atrial Fibrillation and Heart Failure

Follow-up Visits



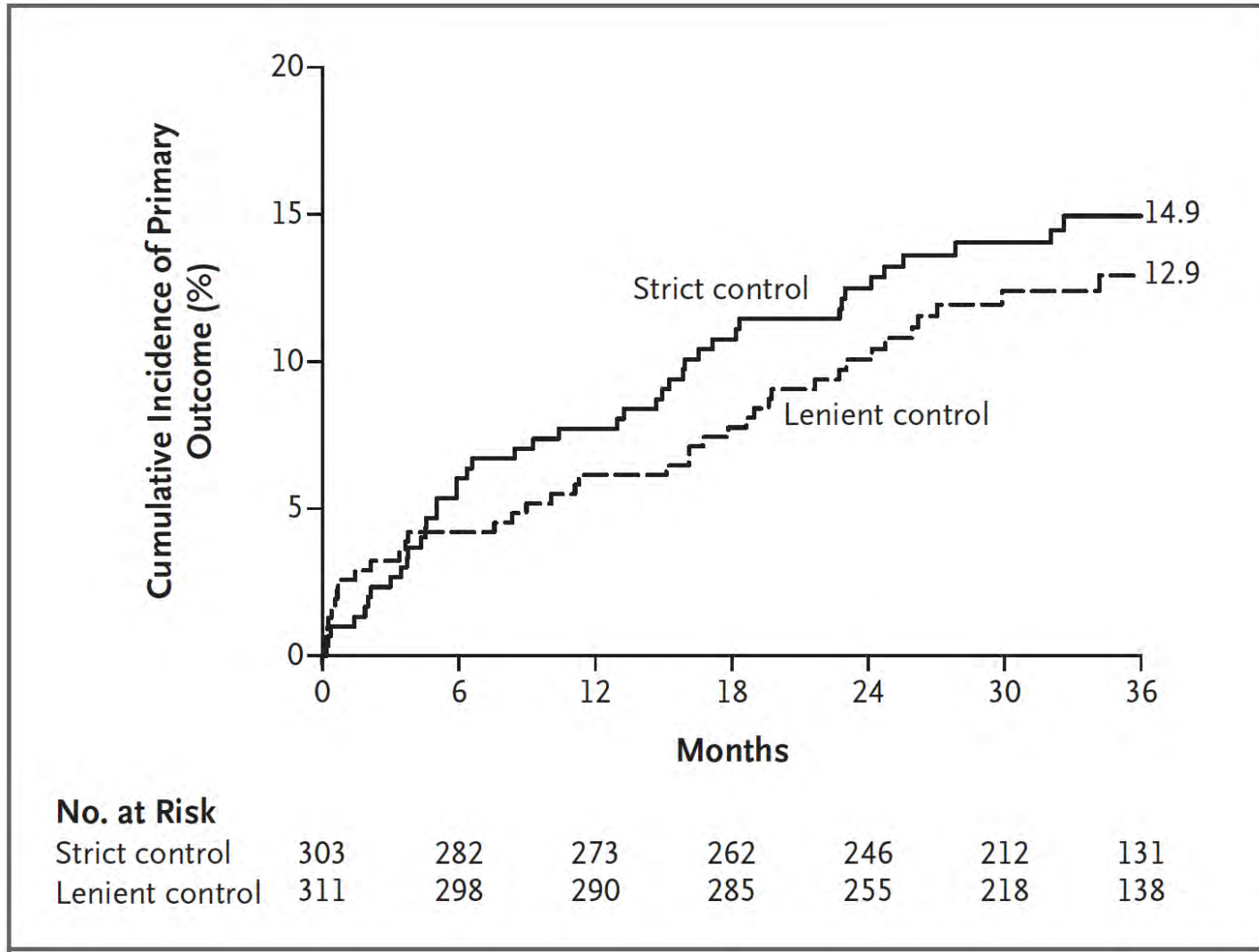
Rhythm Control versus Rate Control for Atrial Fibrillation and Heart Failure



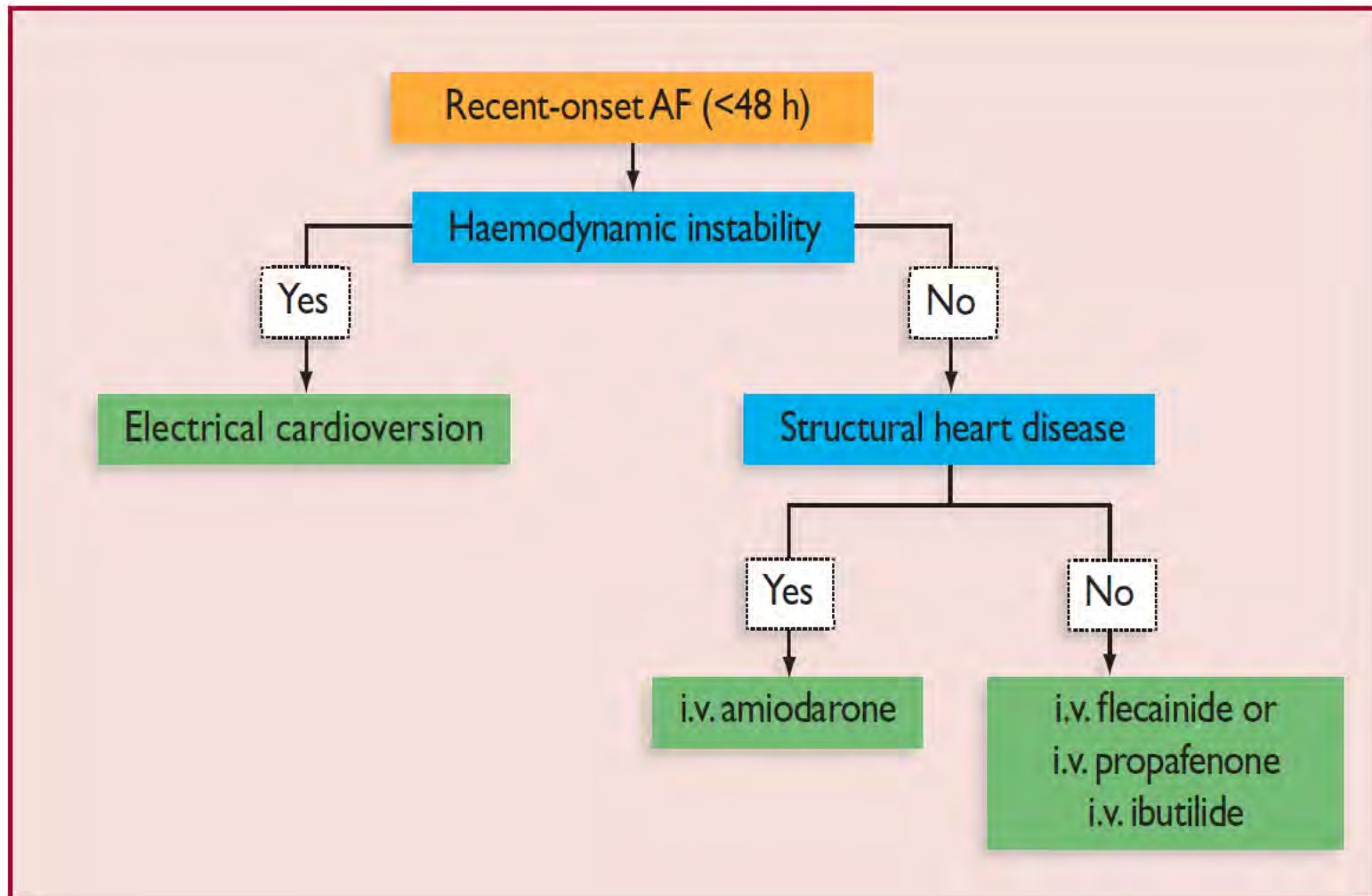
No. at Risk

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

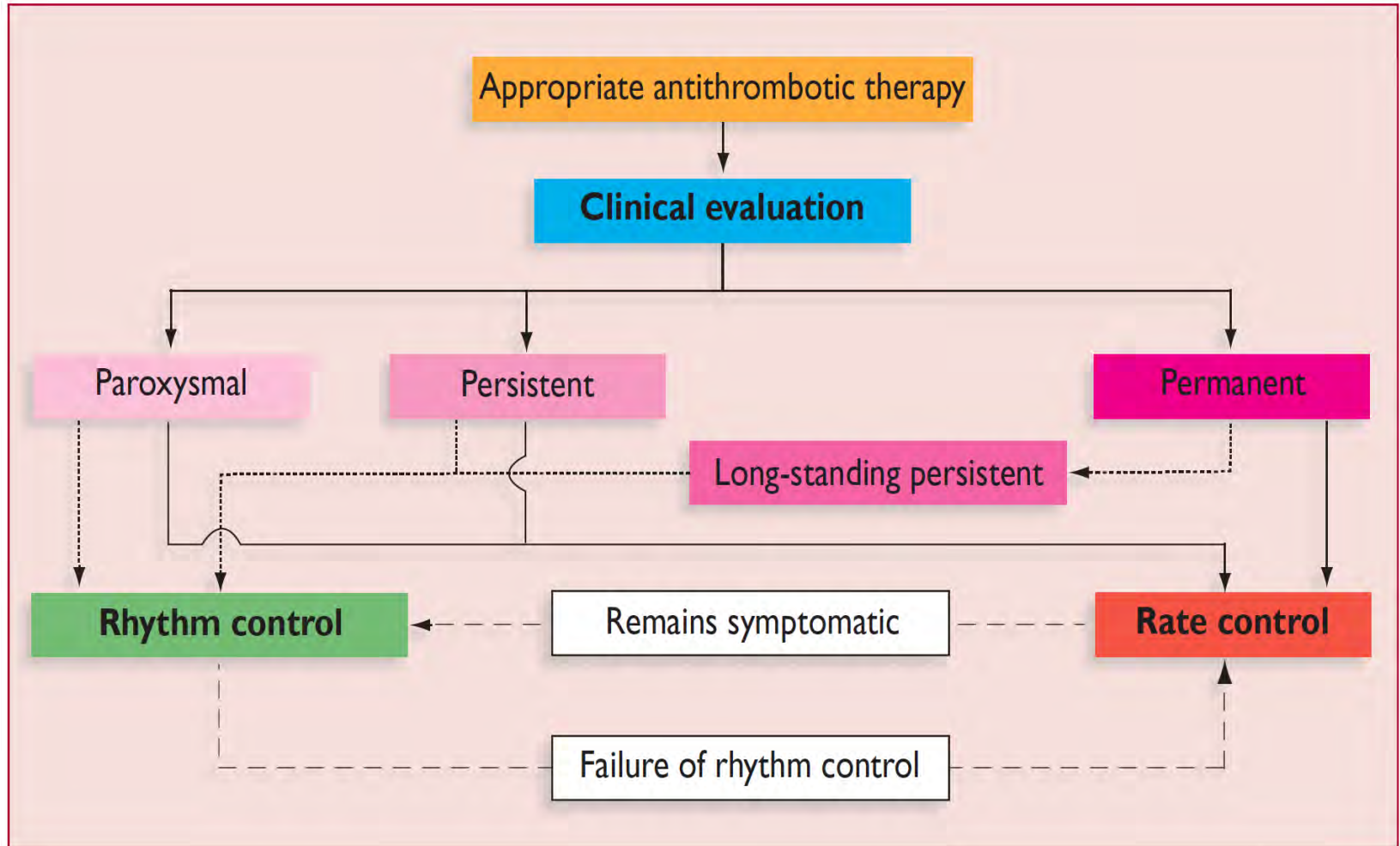
Lenient versus Strict Rate Control in Patients with Atrial Fibrillation



Direct current conversion and pharma-cological cardioversion of recent-onset AF in patients considered for pharmacological cardioversion

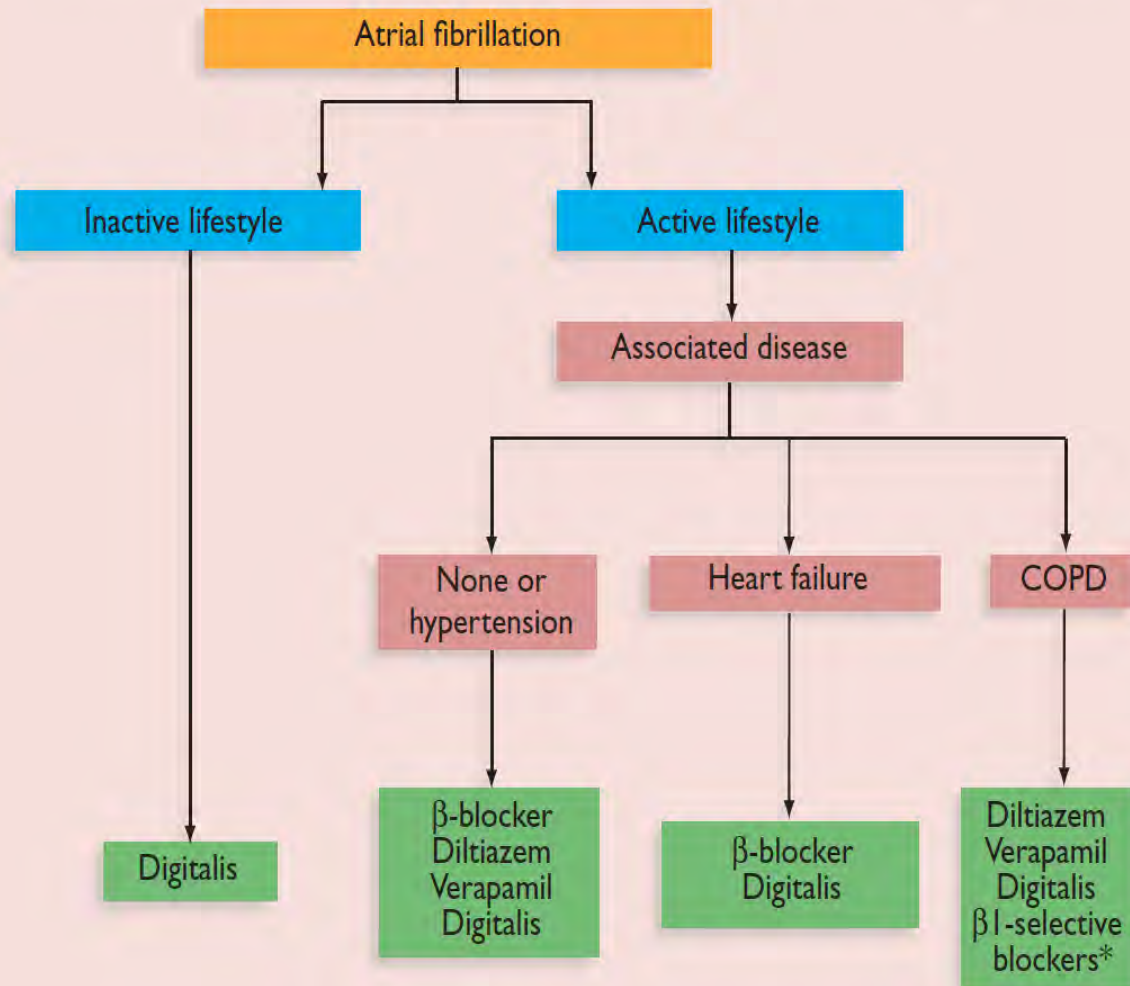


Choice of rate and rhythm control strategies

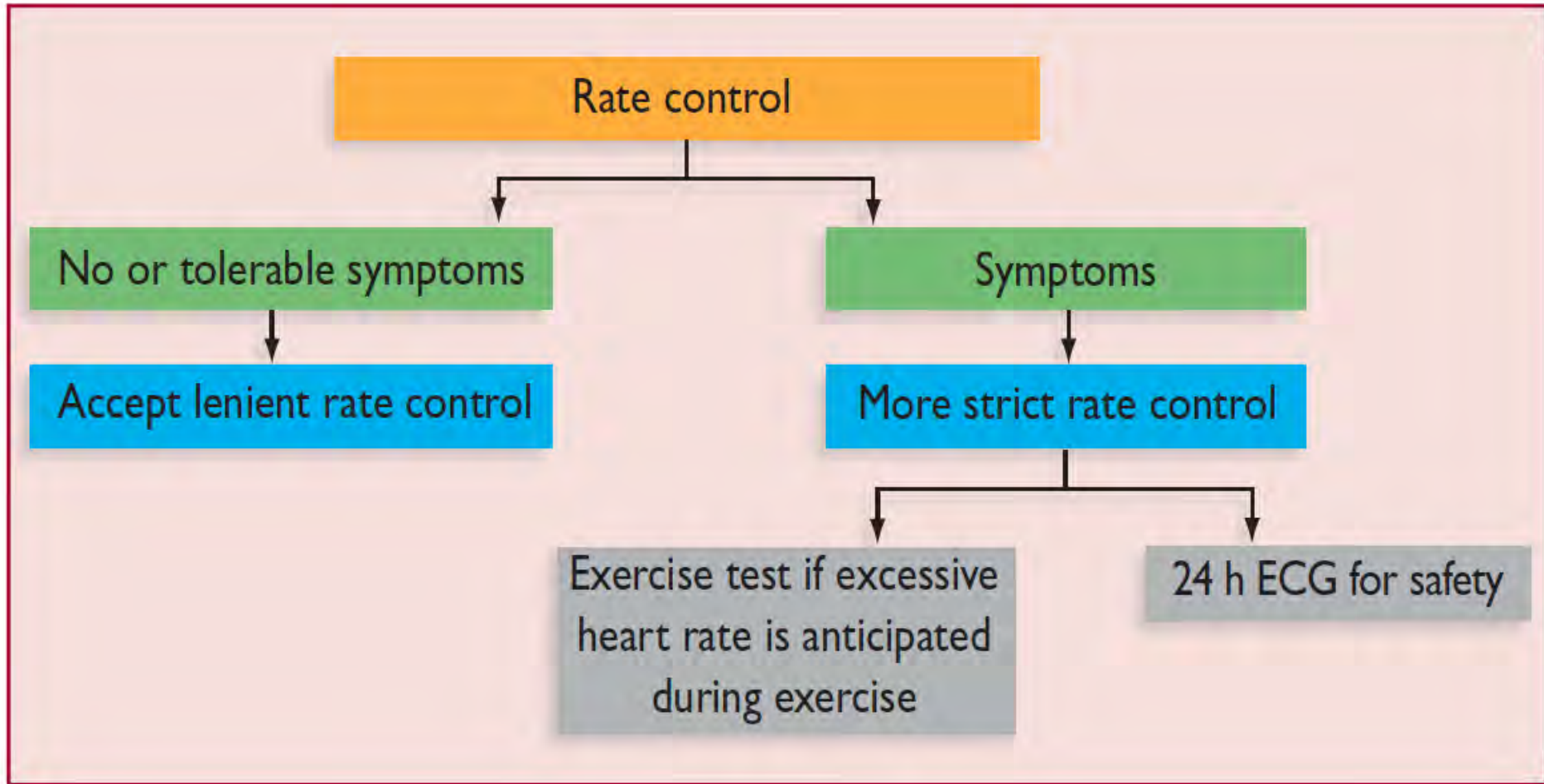


Rate Control

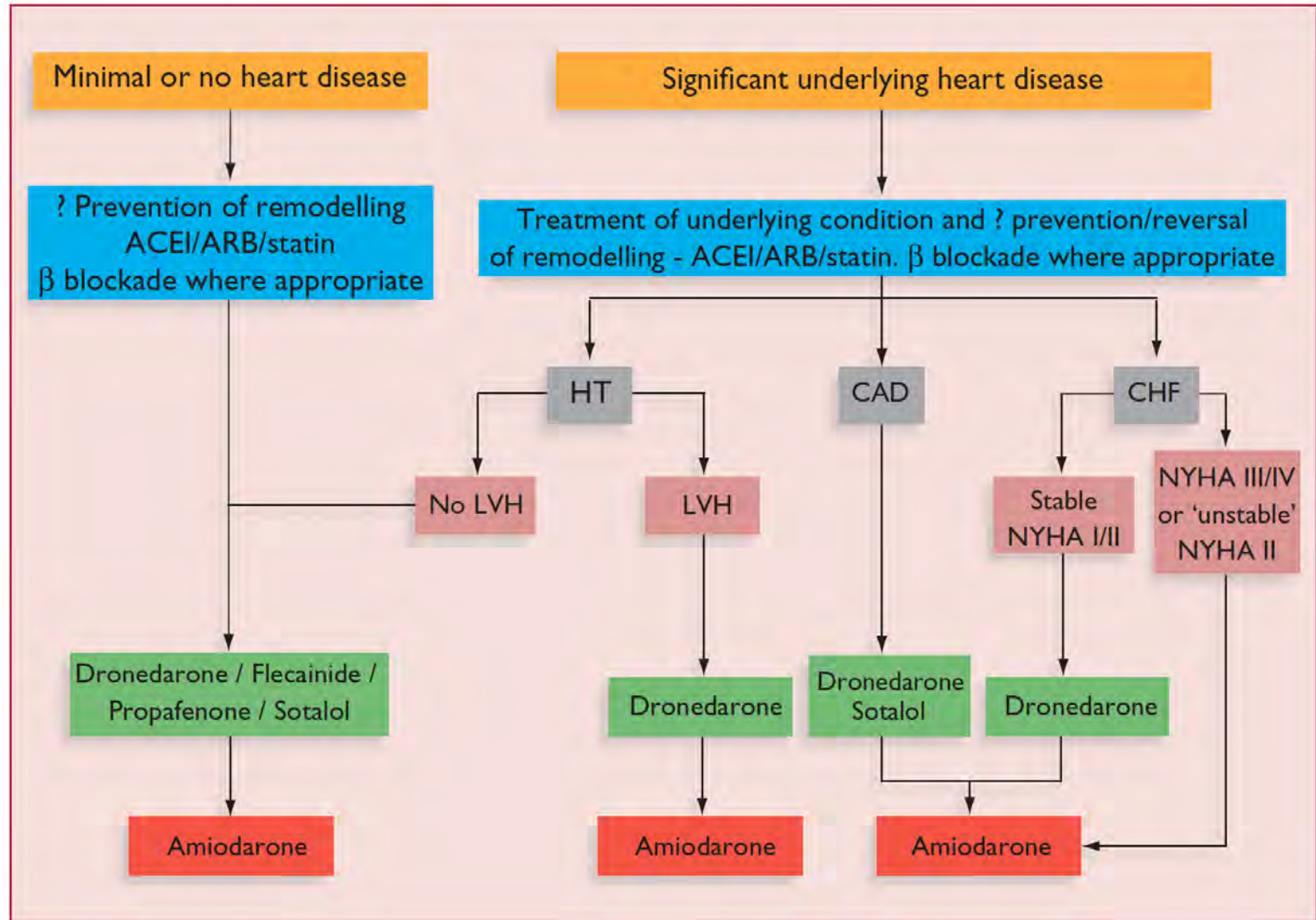
The choice of drugs depends on life-style and underlying disease



Optimal level of heart rate control



Choice of antiarrhythmic drug according to underlying pathology



Merci



Frank Ruschitzka, MD, FRCP, FESC
Professor of Cardiology
University Hospital
Zürich, Switzerland
E-mail: frank.ruschitzka@usz.ch

Cox Multivariable Proportional Hazards Models of 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)

Perception is reality





Risikofaktoren für thromboembolische Ereignisse bei Vorhofflimmern

Risikofaktoren	Relatives Risiko
Anamnese für TIA oder Schlaganfall	2.5
Diabetes mellitus	1.7
Anamnese einer Hypertonie	1.6
Manifeste Herzinsuffizienz	1.4
Alter (pro Dekade)	1.4

M. P.

80 j. Patient mit progredienter Dyspnoe seit 8 Monaten (NYHA III), keine Orthopnoe

2x Elektrokonzersion 2002/2003 bei Vorhofflimmern

Comorbiditäten: hypokinetisches Parkinsonsyndrom

Klinik: BD 82/50 mmHg, HF 130/min, regelmässig.

Malleolarödeme beidseits, Halsvenen nicht gestaut, HJR positiv.

Basale RGs beidseits. Leber 2cm unter RB, 10 cm in MCL.

Was sind die kardialen Probleme des Patienten ?

Systematische Problemanalyse:

- Atemnot**
- bekanntes (St.n.) Vorhofflimmern**
- arterielle Hypotonie**
- Tachykardie**
- Ödeme/HJR positiv**

NYHA Stadien:

NYHA I: Keine körperliche Einschränkung. Alltägliche körperliche Belastung verursacht keine inadäquate Erschöpfung, Rhythmusstörungen, Luftnot oder Angina pectoris.

NYHA II: Leichte Einschränkung der körperlichen Belastbarkeit. Keine Beschwerden in Ruhe. Erschöpfung, Rhythmusstörungen, Luftnot oder Angina pectoris bei alltäglicher körperlicher Belastung.

NYHA III: Höhergradige Einschränkung der körperlichen Leistungsfähigkeit bei gewohnter Tätigkeit. Keine Beschwerden in Ruhe. Erschöpfung, Rhythmusstörungen, Luftnot oder Angina pectoris bei geringer körperlicher Belastung.

NYHA IV: Beschwerden bei allen körperlichen Aktivitäten und in Ruhe. Bettlägrigkeit.



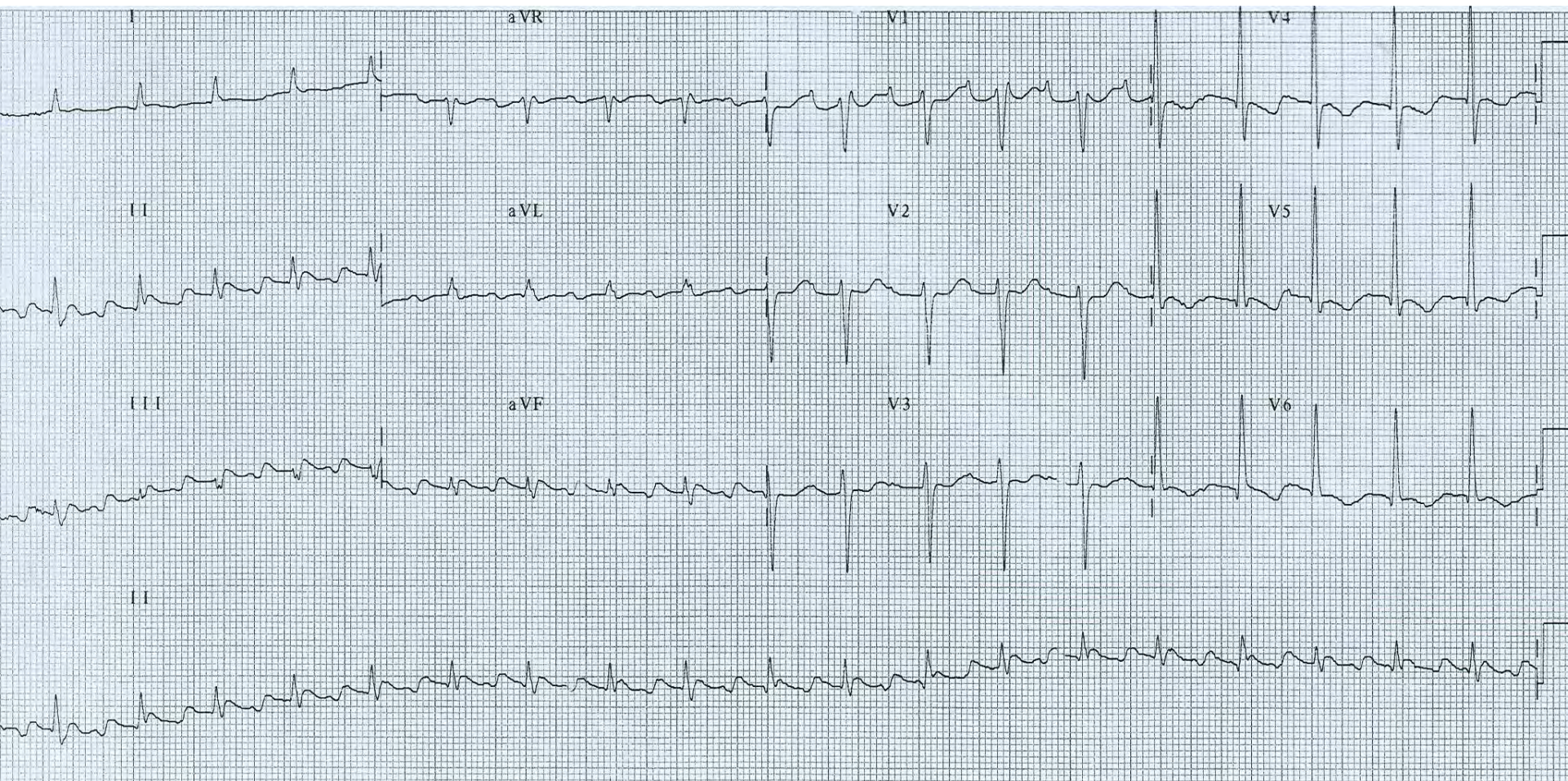
?

Systematische Problemanalyse:

- Atemnot**
- bekanntes (St.n.) Vorhofflimmern**
- arterielle Hypotonie**
- Tachykardie**
- Ödeme/HJR positiv**

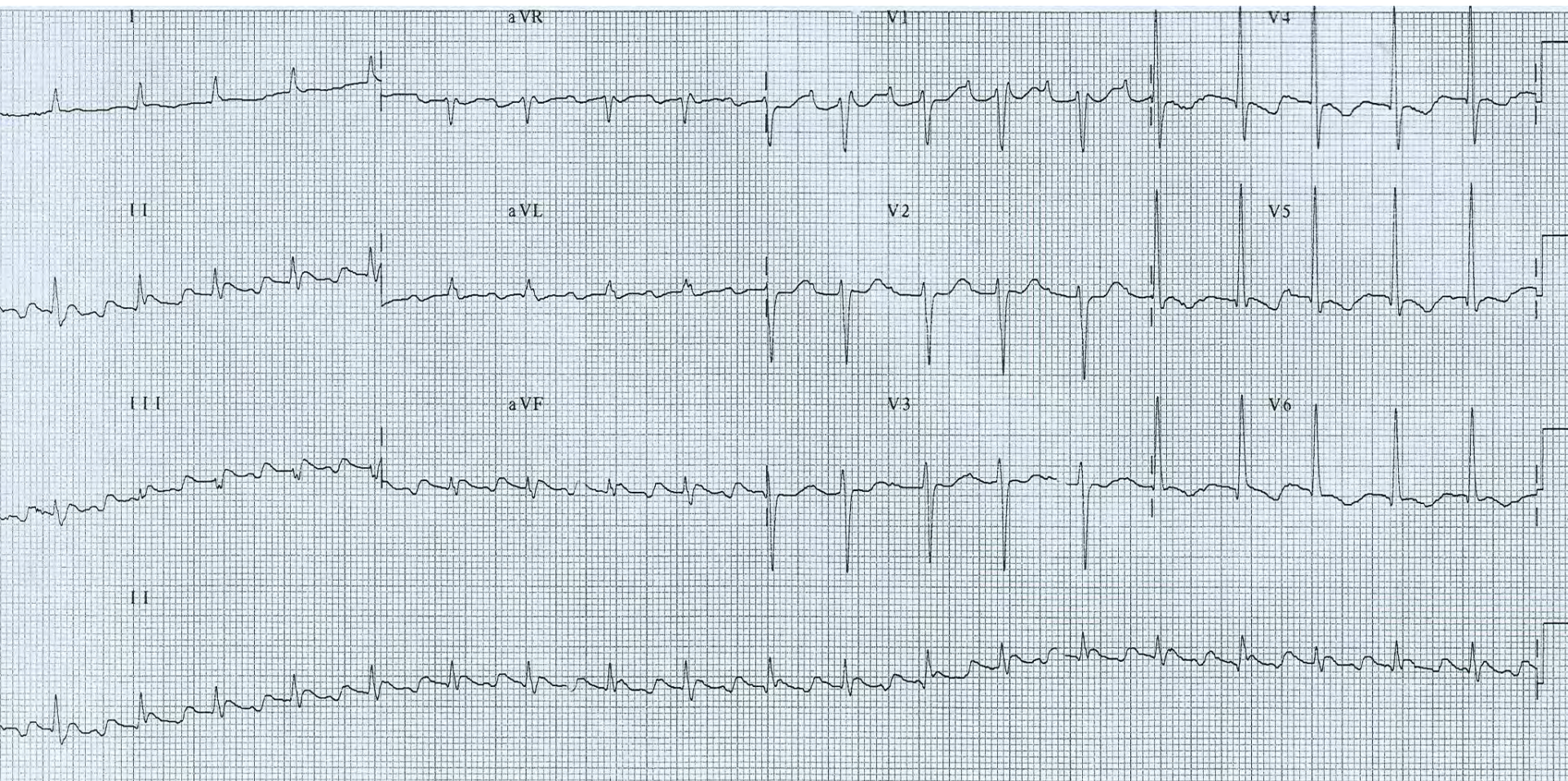
-> nächste Untersuchung?

Ruhe EKG



Ruhe EKG

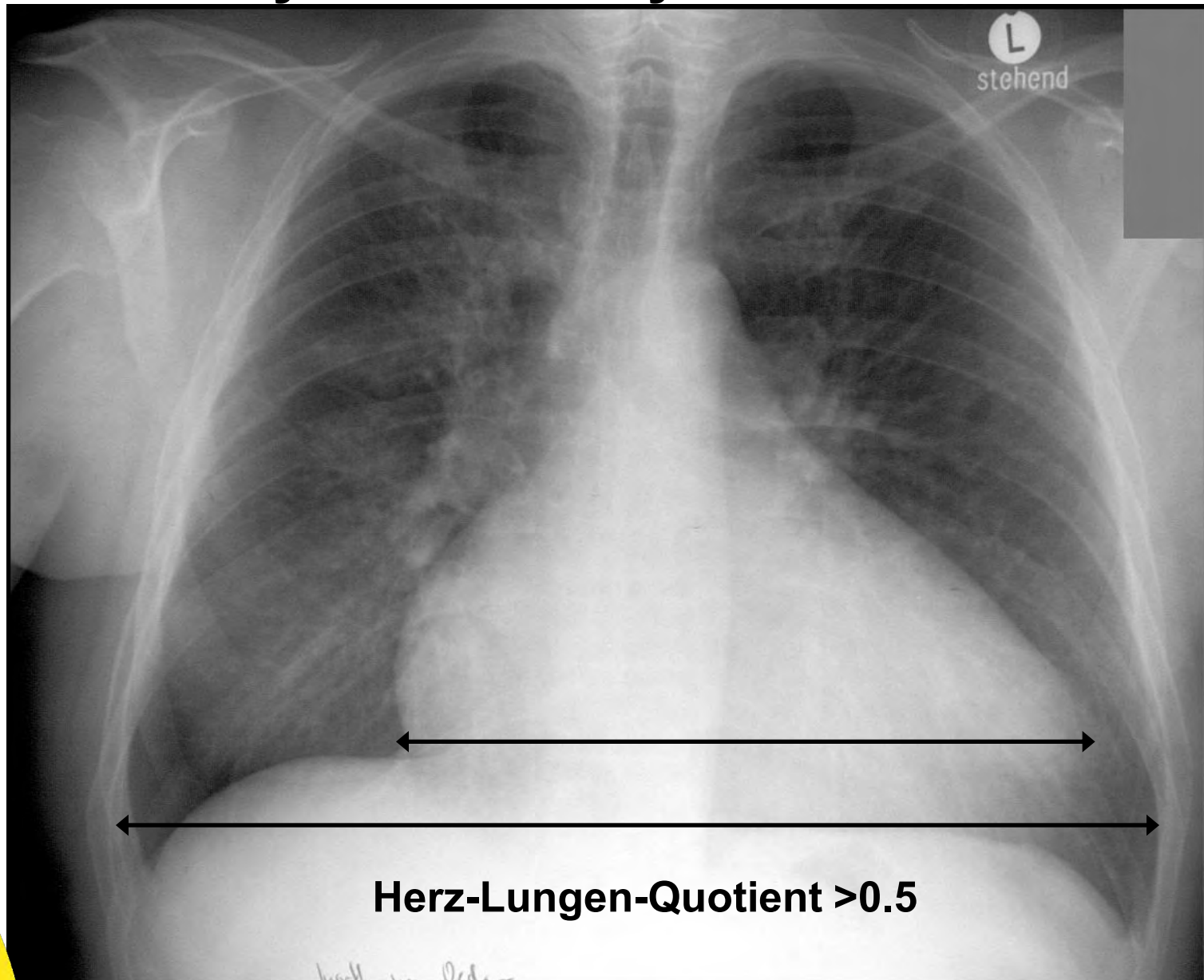
Tachykardes Vorhofflattern (typisch)



Systematische Problemanalyse:

- Atemnot
 - bekanntes (St.n.) Vorhofflimmern
-> aktuell Vorhofflattern!
 - arterielle Hypotonie
 - Tachykardie
 - Ödeme/HJR positiv
- > nächste Untersuchung?

Lungenstauung und Herzvergrößerung bei systolischer Dysfunktion





Eingeschränkte Pumpfunktion



Normale Pumpfunktion



M. P.

80 j. Patient mit progredienter Dyspnoe seit 8 Monaten
NYHA III (bewegt sich wenig, s.u.), keine Orthopnoe
2x Elektrokonzersion 2002/2003 bei Vorhofflimmern

- Vorhofflattern (paroxysmal/chronisch?)

- hämodynamisch wirksam (Hypotonie)
- biventrikuläre kardiale Dekompensation

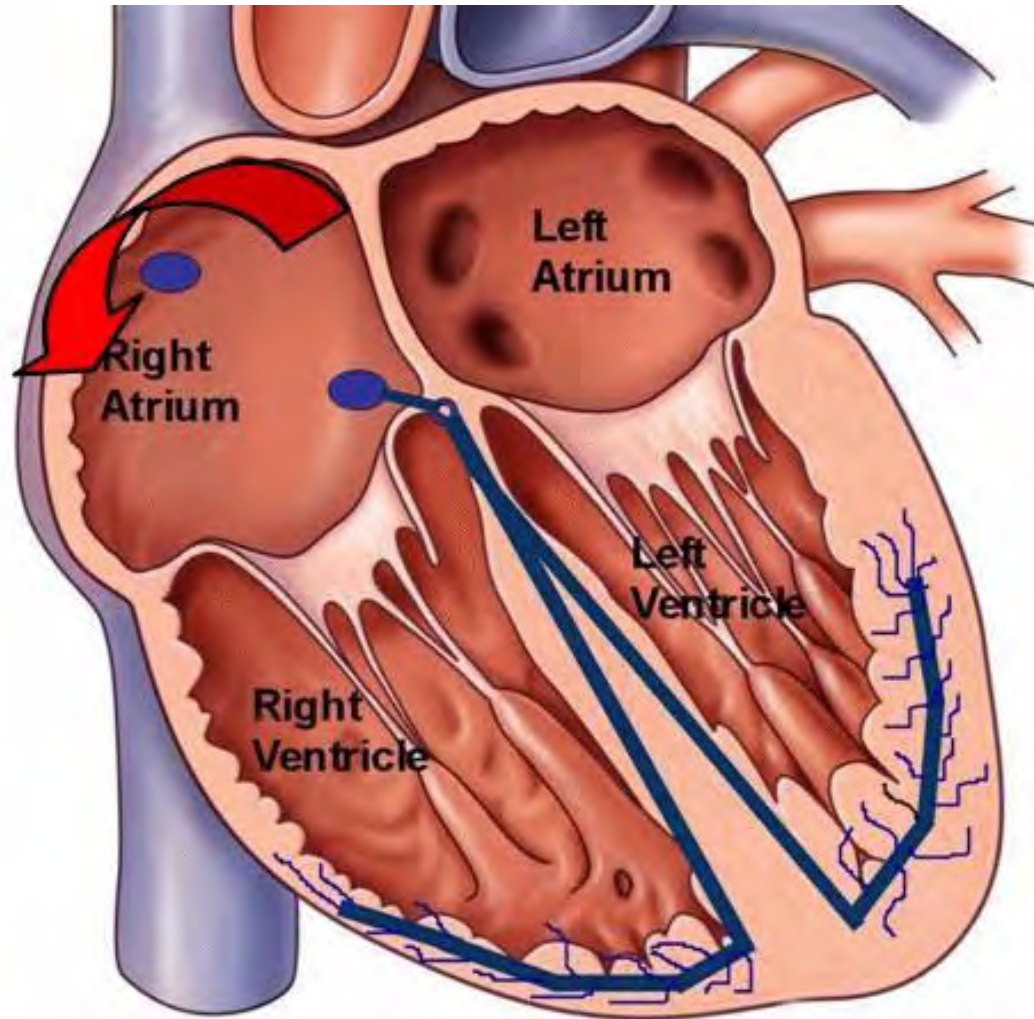
Wie weiter?

Was ist das Vorhofflattern/flimmern?

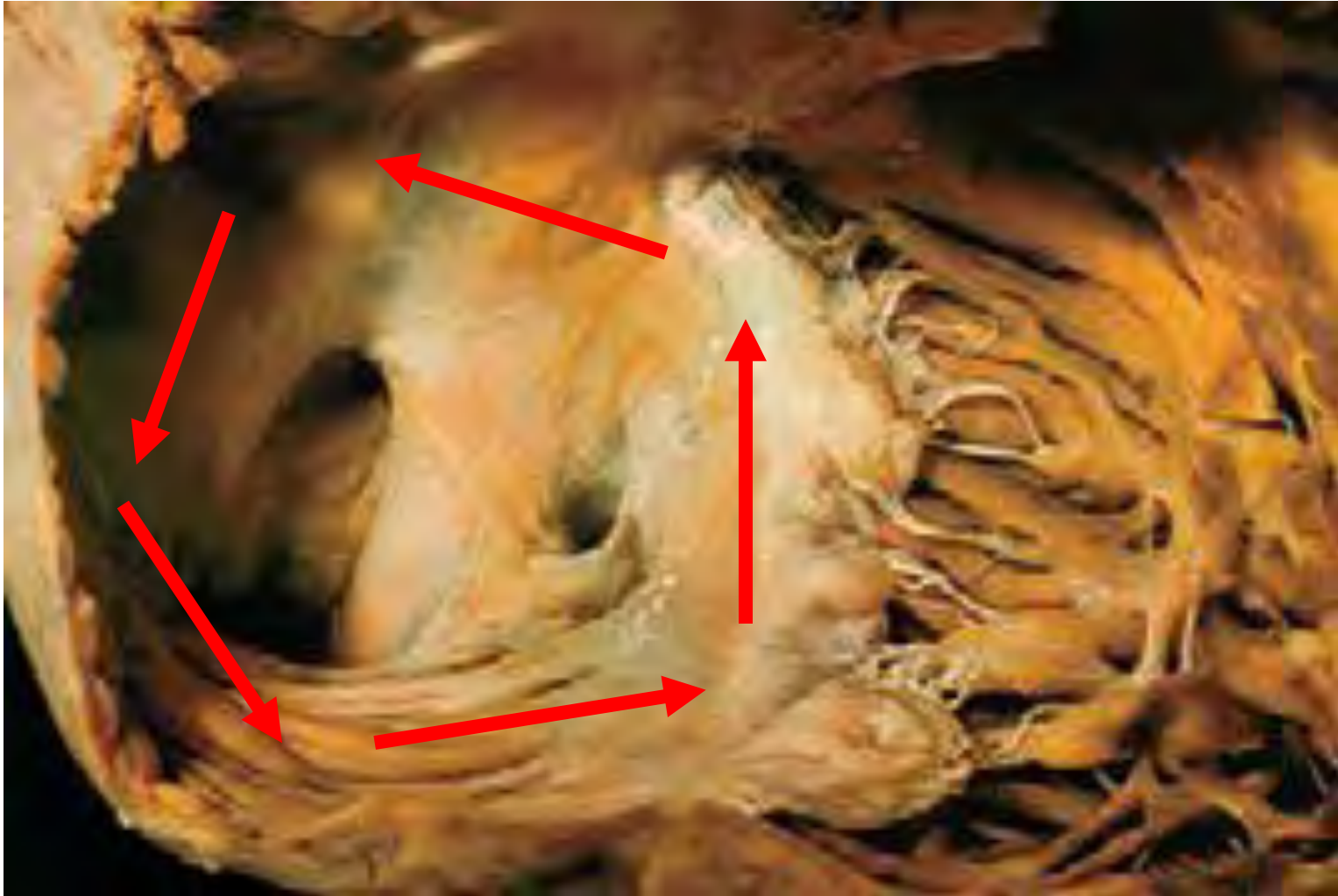
Gefahren des Vorhofflattern/-flimmerns?

Was braucht der Patient für Medikamente ?

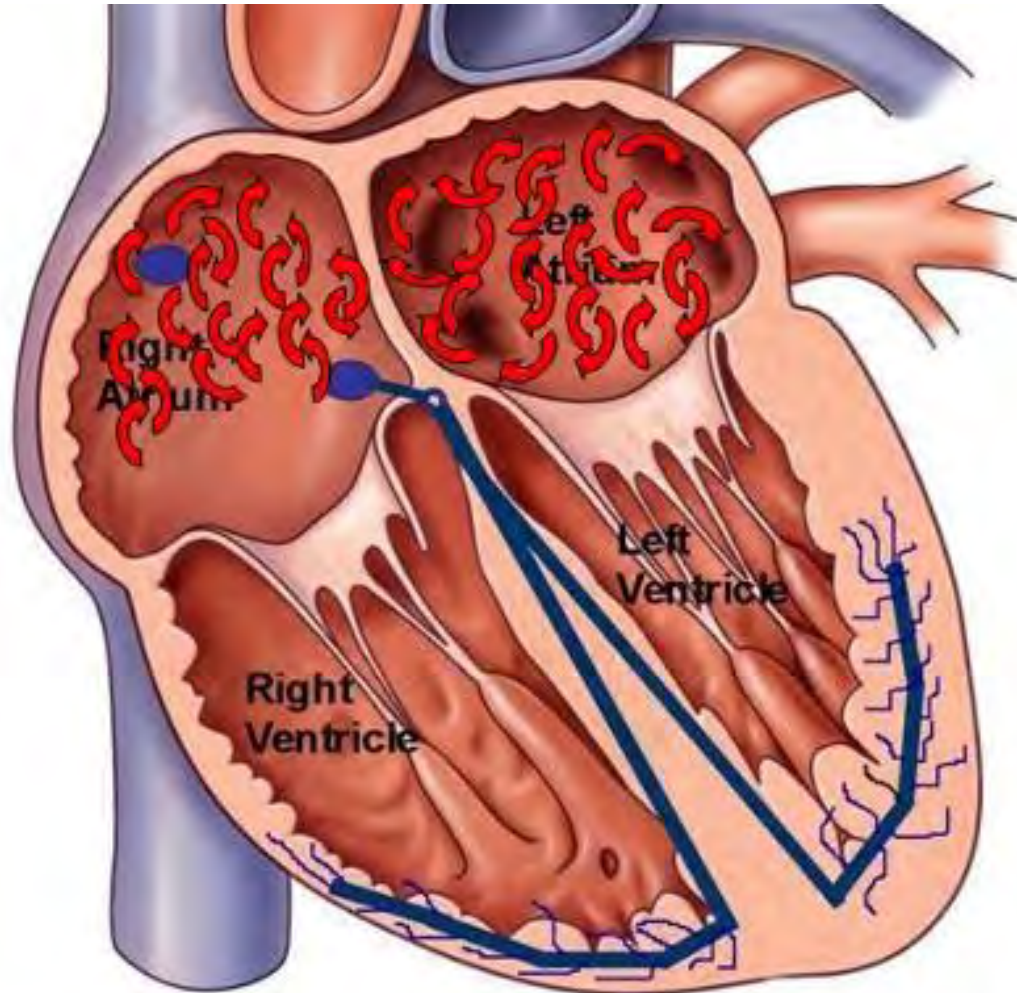
Was ist Vorhofflattern?



Was ist Vorhofflattern?



Was ist Vorhofflimmern?



EMEDU

I

aVR

V1

V4

II

aVL

V2

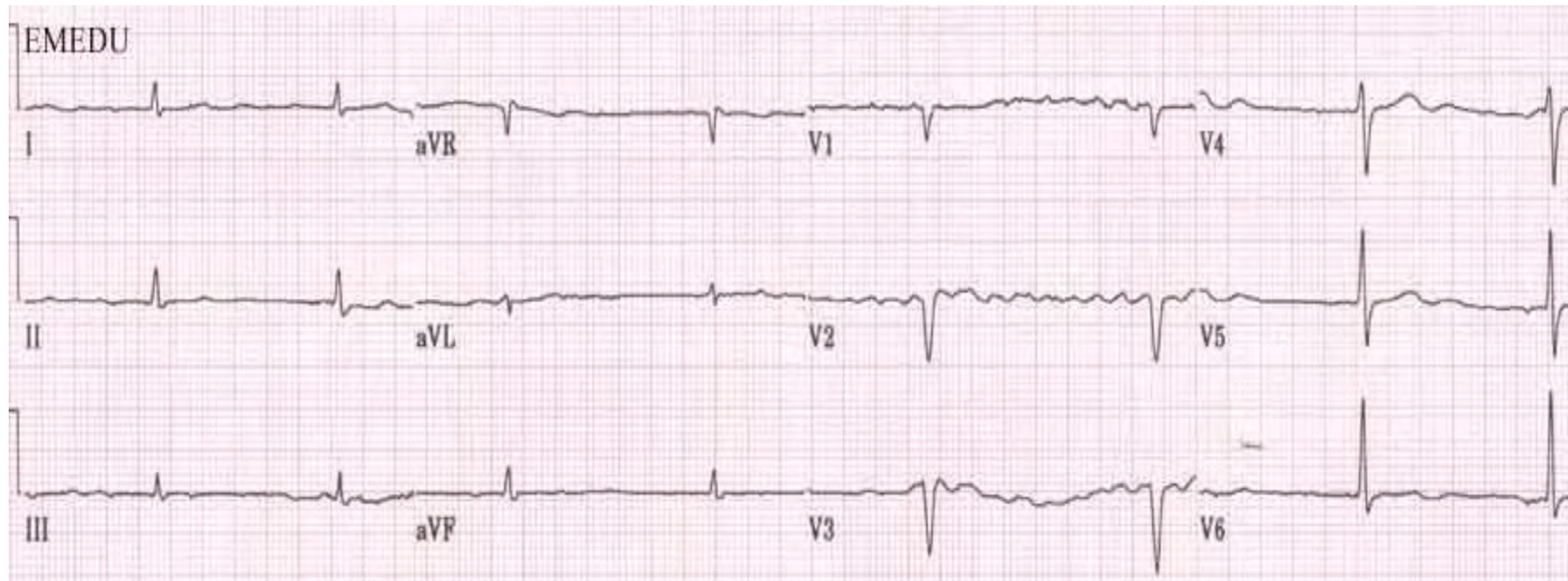
V5

III

aVF

V3

V6



Definition von AFib

Vorhofflimmern ist gemäss den neuesten ACC/AHA/ESC-Richtlinien definiert als

supraventrikuläre Tachyarrhythmie, die durch eine unkoordinierte atriale Aktivierung mit dadurch bedingter Verschlechterung der mechanischen Vorhoffunktion gekennzeichnet ist.

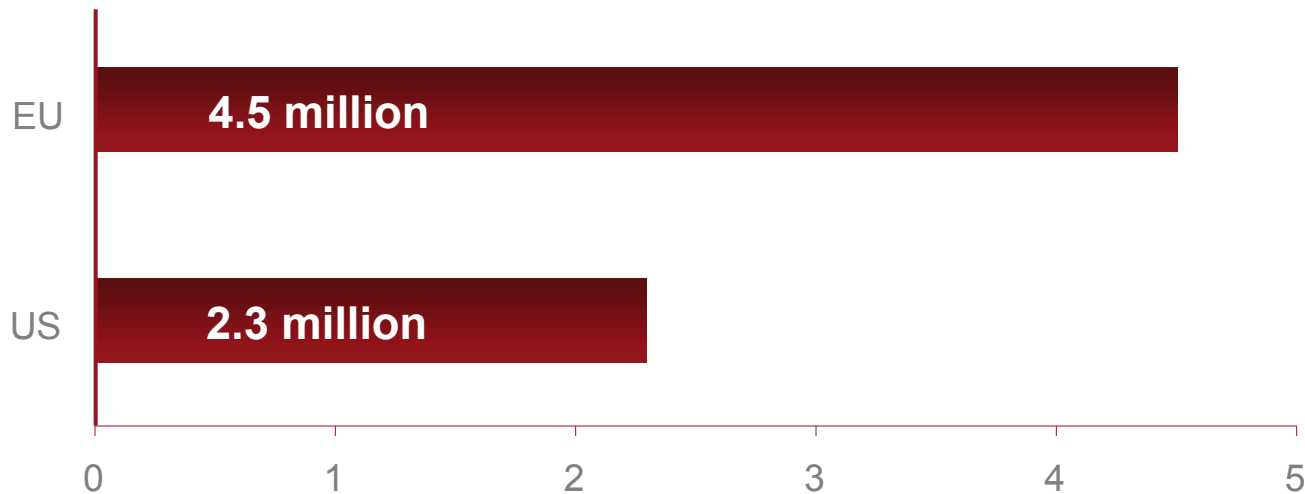
Klassifikation von AFib-Subtypen

Paroxysmal	Spontane Beendigung üblicherweise < 7 Tage und meist < 48 Stunden
Persistierend	Keine spontane Beendigung, benötigt eine therapeutische Intervention zur Beendigung (medikamentöse oder elektrische Kardioversion)
Permanent	AFib, bei der ein Kardioversion versucht wurde, die fehlschlug oder aber nur kurzzeitig erfolgreich war, oder eine Form von AFib, bei der beschlossen wurde, keine Kardioversion zu versuchen

Vorhofflimmern ist die häufigste Herzrhythmusstörung

- Vorhofflimmern betrifft
 - 1 von 25 >60 Jahre¹
 - 1 von 10 >80 Jahre¹

Wie viele Personen weltweit?



* EU 2001, US 2006, both cited in 2006 guidelines

1. Go AS, et al. *JAMA* 2001;285:2370-2375.

2. Fuster V, et al. *J Am Coll Cardiol*. 2006;38:1231-1265.

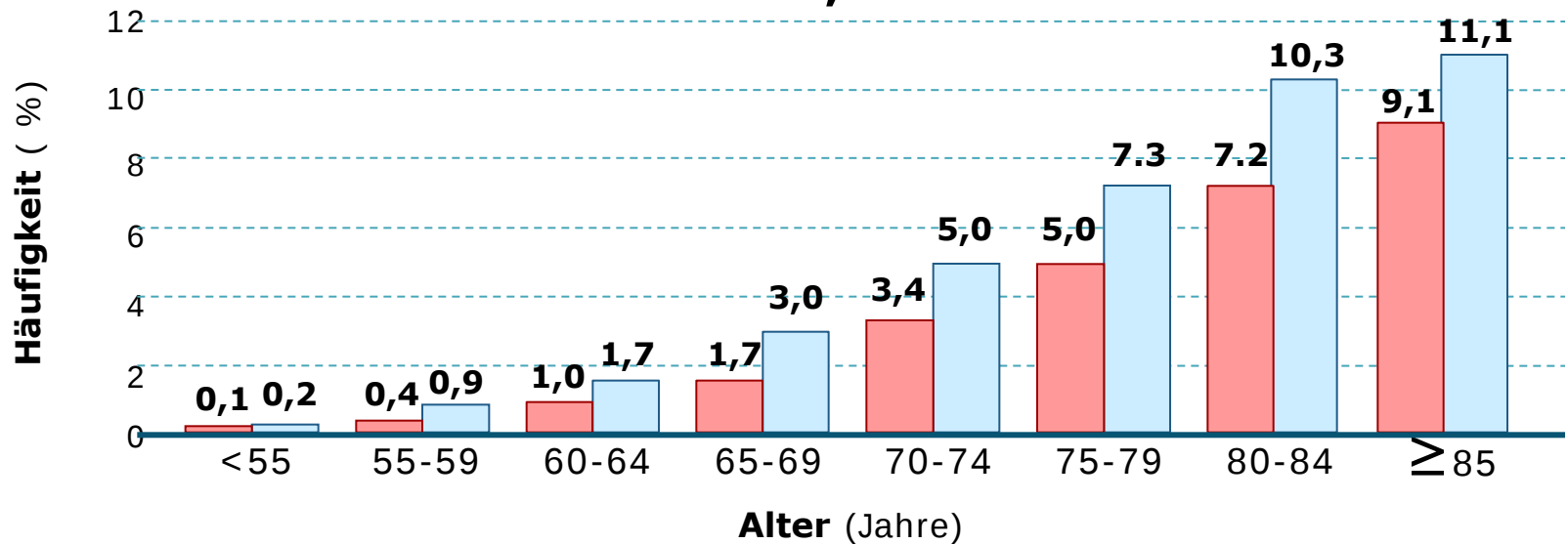
Prävalenz von AFib, nach Alter und Geschlecht stratifiziert

ATRIA Studie

Männer 1,1 % Frauen 0,8 %

■ Frauen
■ Männer

Mittelwert 0,95 %



Anzahl								
Frauen	530	310	566	896	1498	1572	1291	1132
Männer	1259	634	934	1426	1907	1886	1374	759

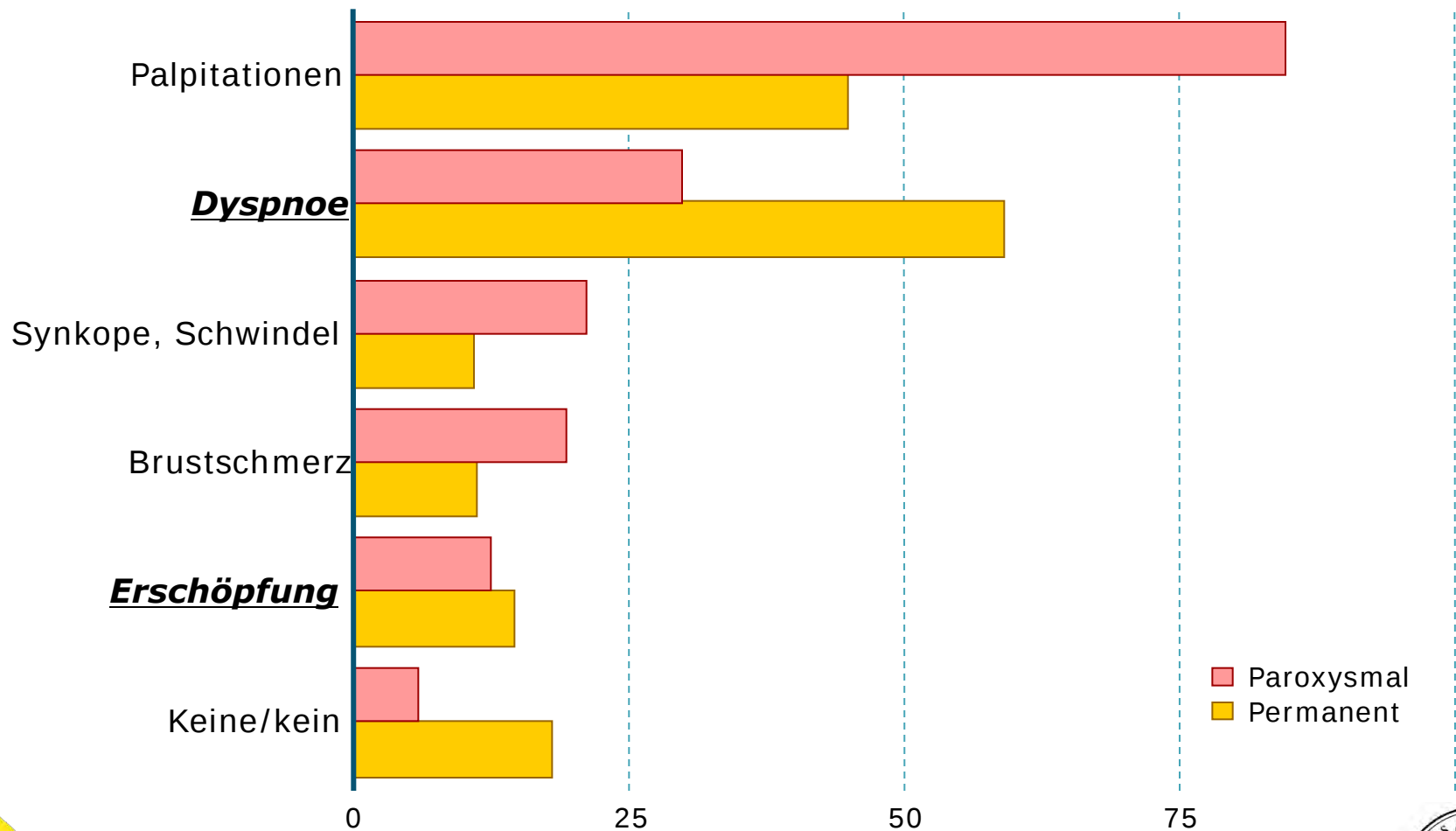
Inzidenz von AFib – Lebensdauerisiko

Framingham-Studie – Lebensdauerisiko 1 von 4 für eine Entwicklung von AFib

- **8725 im Alter von 40 Jahren AFib-freie Patienten wurden im Zeitraum von 1968-1999 beobachtet**
- **Lebensdauerisiko für die Entstehung von AFib im Alter von 40 Jahren:**
 - **26,0 % bei Männern**
 - **23,0 % bei Frauen**

Symptome von AFib

ALFA-Studie: paroxysmal n=167; permanent/chronisch n=389



M. P.

80 j. Patient mit progredienter Dyspnoe seit 8 Monaten
NYHA III (bewegt sich wenig, s.u.), keine Orthopnoe
2x Elektrokonzersion 2002/2003 bei Vorhofflimmern

- **Vorhofflattern (paroxysmal/chronisch?)**

- hämodynamisch wirksam (Hypotonie)
- biventrikuläre kardiale Dekompensation

Wie weiter?

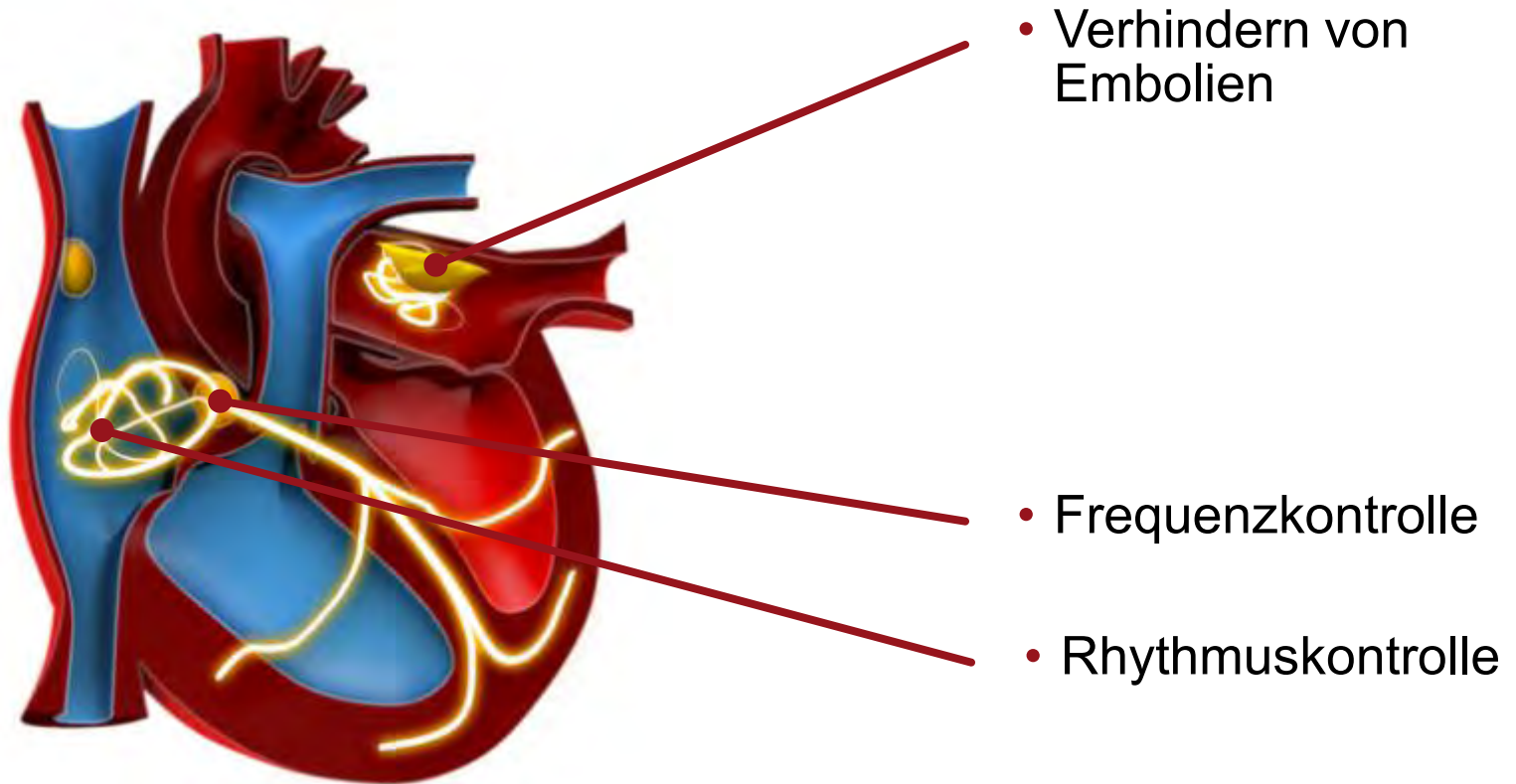
Was ist das Vorhofflattern/flimmern?

Gefahren des Vorhofflattern/-flimmerns?

Was braucht der Patient für Medikamente ?



Current Treatment Strategies for AF



Frage der antithrombotischen Therapie

Risikofaktoren für thromboembolische Ereignisse bei Vorhofflimmern

Risikofaktoren	Relatives Risiko
Anamnese für TIA oder Schlaganfall	2.5
Diabetes mellitus	1.7
Anamnese einer Hypertonie	1.6
Manifeste Herzinsuffizienz	1.4
Alter (pro Dekade)	1.4

CHADS2 Score

CHADS2 score, thromboembolic risk, and effect of warfarin in 11,526 patients with nonvalvular atrial fibrillation and no contraindications to warfarin therapy

Clinical parameter			Points
Congestive heart failure (any history)			1
Hypertension (prior history)			1
Age ≥ 75 years			1
Diabetes mellitus			1
Secondary prevention in patients with a prior ischemic stroke or a transient ischemic attack; most experts also include patients with a systemic embolic event			2
CHADS2 score	Events per 100 person-years*		NNT
	Warfarin	No warfarin	
0	0.25	0.49	417
1	0.72	1.52	125
2	1.27	2.50	81
3	2.20	5.27	33
4	2.35	6.02	27
5 or 6	4.60	6.88	44

NNT: number needed to treat to prevent one stroke per year with warfarin

CHADS₂ Score and Stroke Rate

CHADS ₂ score	Patients (n=1733)	Adjusted stroke rate (%/year) ^a (95% confidence interval)
0	120	1.9 (1.2–3.0)
1	463	2.8 (2.0–3.8)
2	523	4.0 (3.1–5.1)
3	337	5.9 (4.6–7.3)
4	220	8.5 (6.3–11.1)
5	65	12.5 (8.2–17.5)
6	5	18.2 (10.5–27.4)

CHADS₂ Risikokriterien

Schlaganfall oder TIA, 2 Punkte

Alter > 75 Jahre, Hypertonie, Diabetes mellitus, kürzlich manifeste Herzinsuffizienz je 1 Punkt

CHADS Risikokriterien zur Abschätzung des Risikos für thromboembolische Ereignisse bei nicht valvulärem Vorhofflimmern

Patienten (n=1733) Keine OAK	Schlaganfälle %/Jahr (95%CI)	CHADS2 score
120	1.9 (1.2-3.9)	0
463	2.8 (2.0-3.8)	1
523	4.0 (3.1-5.1)	2
337	5.9 (4.6-7.3)	3
220	8.5 (6.3-11.1)	4
65	12.5 (8.2-17.5)	5
5	18.2 (10.5-27.4)	6

CHADS2 Risikokriterien

Schlaganfall oder TIA, 2 Punkte

Alter > 75 Jahre, Hypertonie, Diabetes mellitus, kürzlich manifeste
Herzinsuffizienz je 1 Punkt

CHADS Risikokriterien zur Abschätzung des Risikos für thromboembolische Ereignisse bei nicht valvulärem Vorhofflimmern

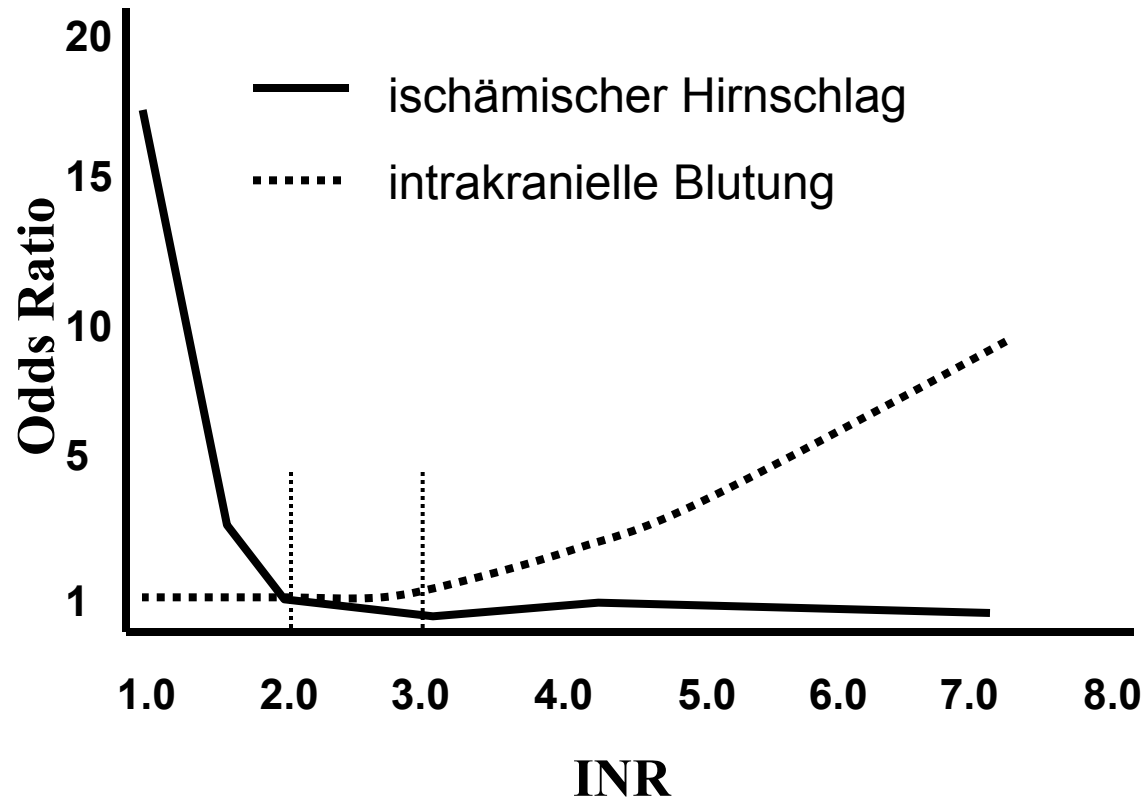
Patienten (n=1733) Keine OAK	Schlaganfälle %/Jahr (95%CI)	CHADS2 score
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CHADS2 Risikokriterien

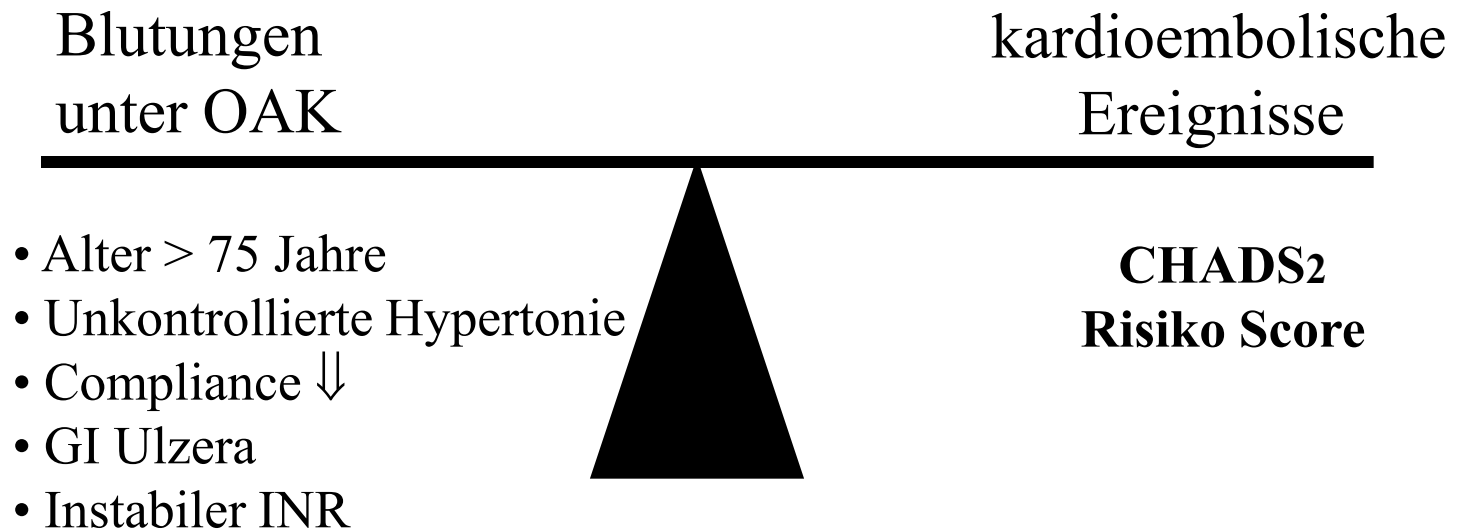
Schlaganfall oder TIA, 2 Punkte

Alter > 75 Jahre, Hypertonie, Diabetes mellitus, kürzlich manifeste
Herzinsuffizienz je 1 Punkt

Vorhofflimmern: Ereignisse unter oraler Antikoagulation



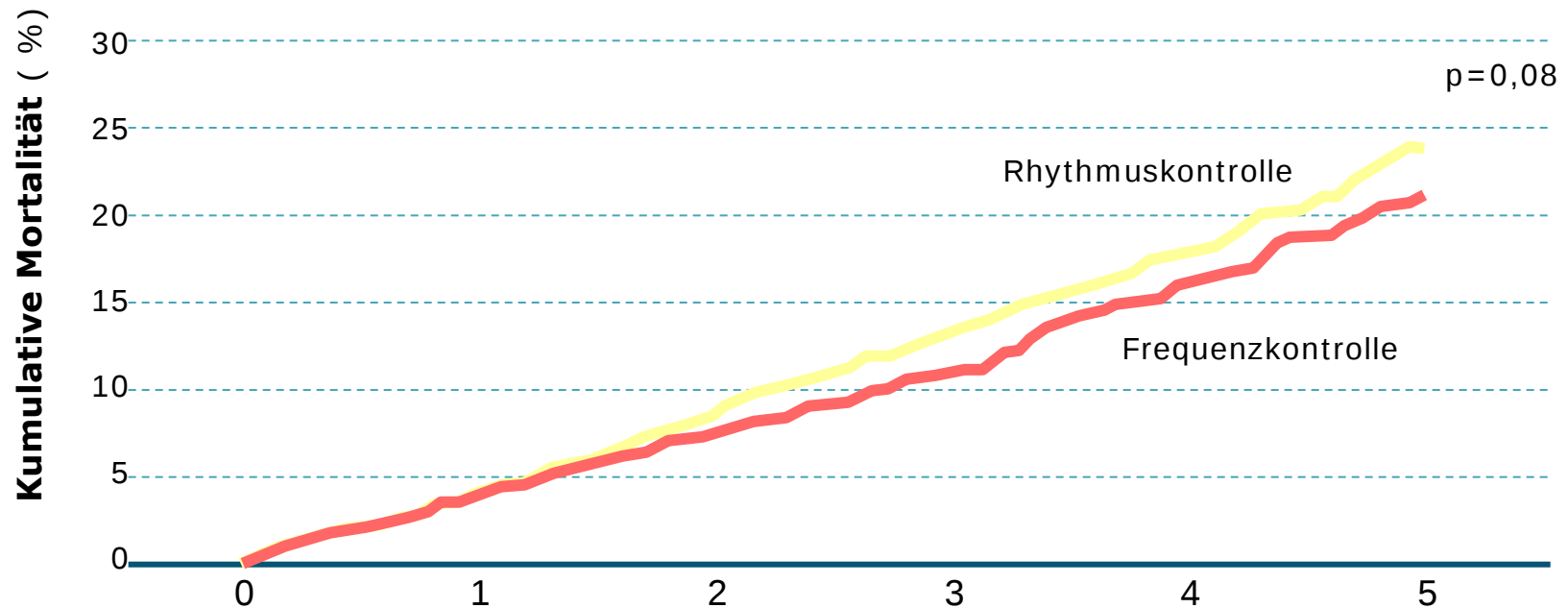
Risikofaktoren für thromboembolische Ereignisse und Blutungen unter antithrombotischer Therapie



Congestive heart failure, **H**ypertension, **A**ge >75 years, **D**iabetes mellitus, and prior **S**troke or TIA

Afib-Folgeuntersuchung des Rhythmusmanagements (AFFIRM)

Kein Überlebensvorteil von Rhythmuskontrolle gegenüber Frequenzkontrolle (n=4060)



Anz. Todesfälle

Jahre

	0	1	2	3	4	5
Rhythmuskontrolle	0	80 (4)	175 (9)	357 (13)	314 (18)	352 (24)
Frequenzkontrolle	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

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Wie weiter?

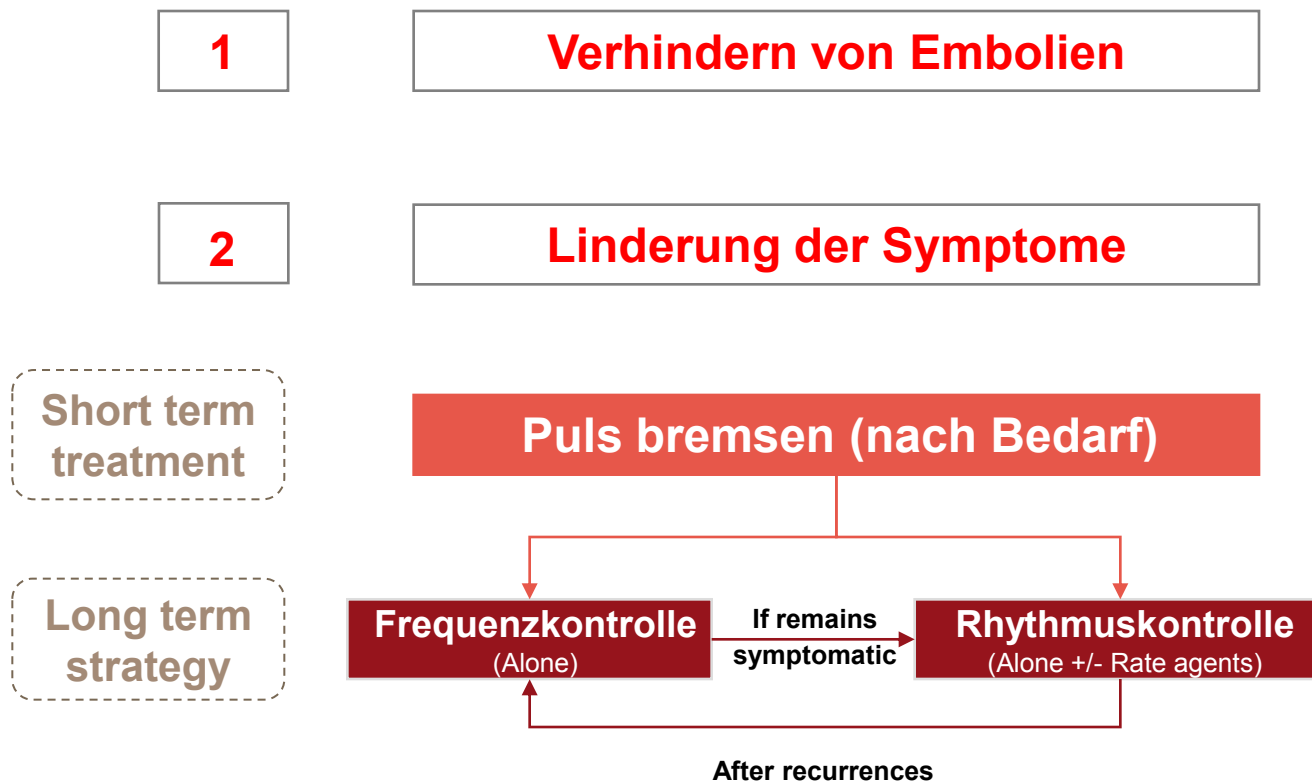
Was ist das Vorhofflattern/flimmern?

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Behandlungsstrategien des Vorhofflimmerns



Therapie des typischen Vorhofflatterns

Tachykardes Vorhofflattern

Frequenz kontrollieren ?

- z.B. Betablocker steigern -> Ziel: 3-4:1 Überleitung

Rhythmus kontrollieren ?

- **Kardioversion**
 - elektrisch: bereits mehrmals erfolglos
 - medikamentös: ?
- **Radiofrequenzablation**

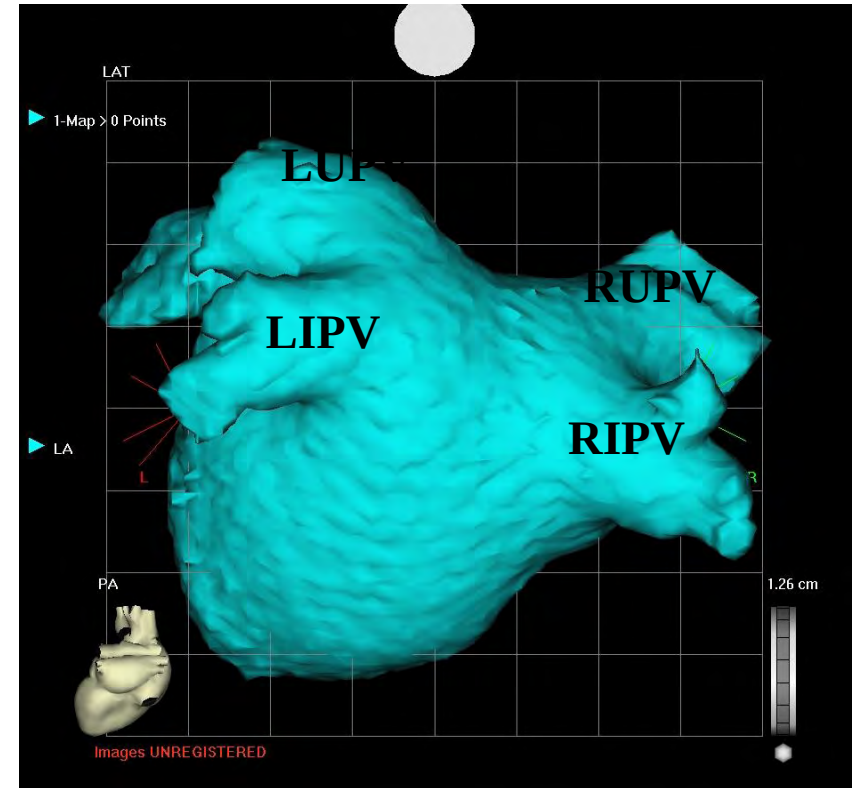
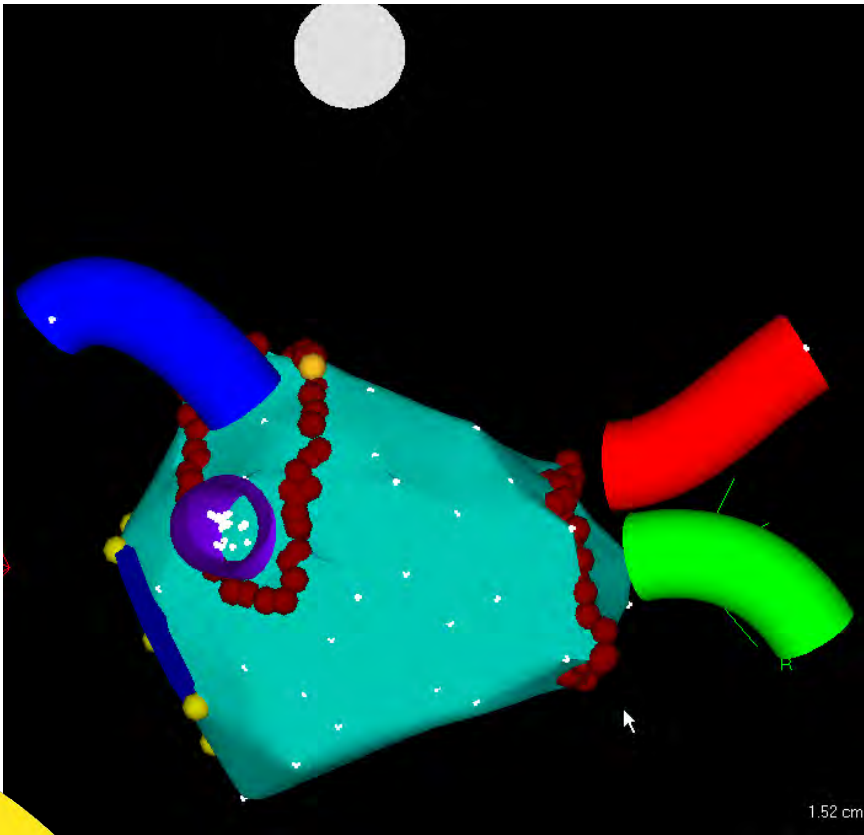
Vorhofflattern



Bei unregelmässiger oder auch 2:1 Überleitung sind nicht immer alle P-Wellen sichtbar

3D-Mapping + Bildgebung (Imaging)

CARTO™



CT

Ansichten von posterior

Zirkuläre Mappingkatheter (LASSO®)

Präzises Mapping von Potentialen und Ausgangsstellen an PV

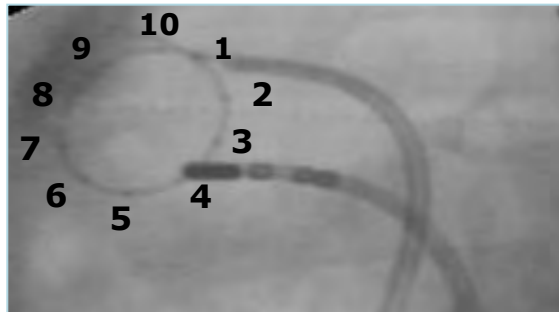
**Vollständig
zusammengezogen**
15 mm



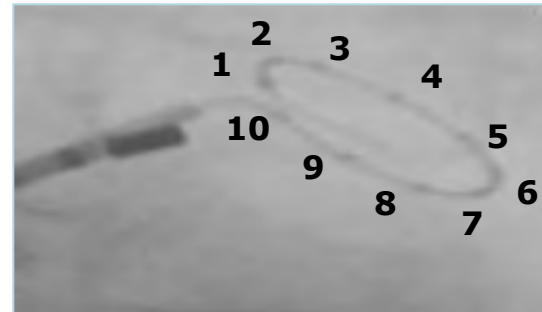
**Vollständig
ausgefahren**
25 mm



RSPV-Mapping

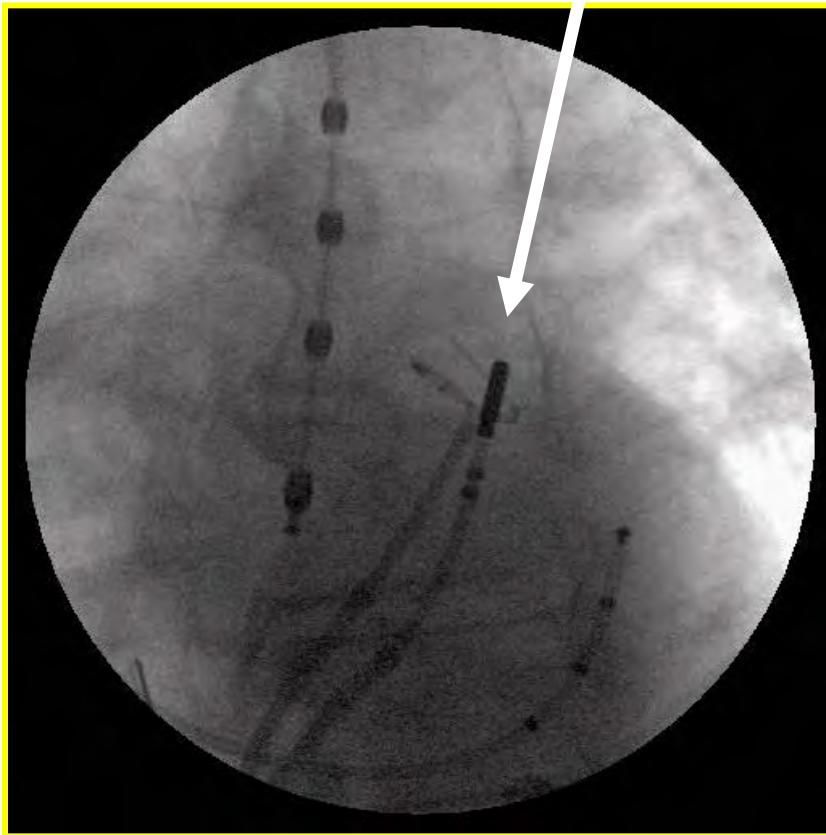


LSPV-Mapping



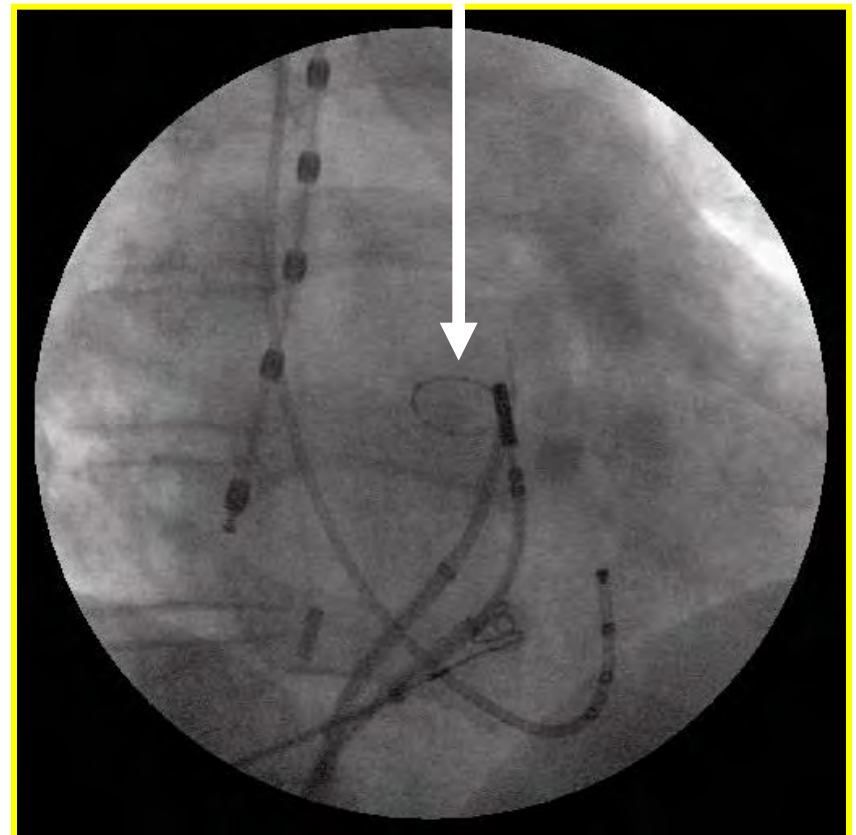
Kathetervisualisierung mit Hilfe von Fluoroskopie

Ablationskatheter



LAO

Lasso®



RAO

Energiequellen

- Hochfrequenzstrom
 - Häufigste Energiequelle
- Cryoablation
- Ultraschall
- Laser
- Mikrowelle

Radiofrequenzablation, Technische Aspekte

Wechselspannung, 300 bis 700 kHz, 30 bis 70 Watt

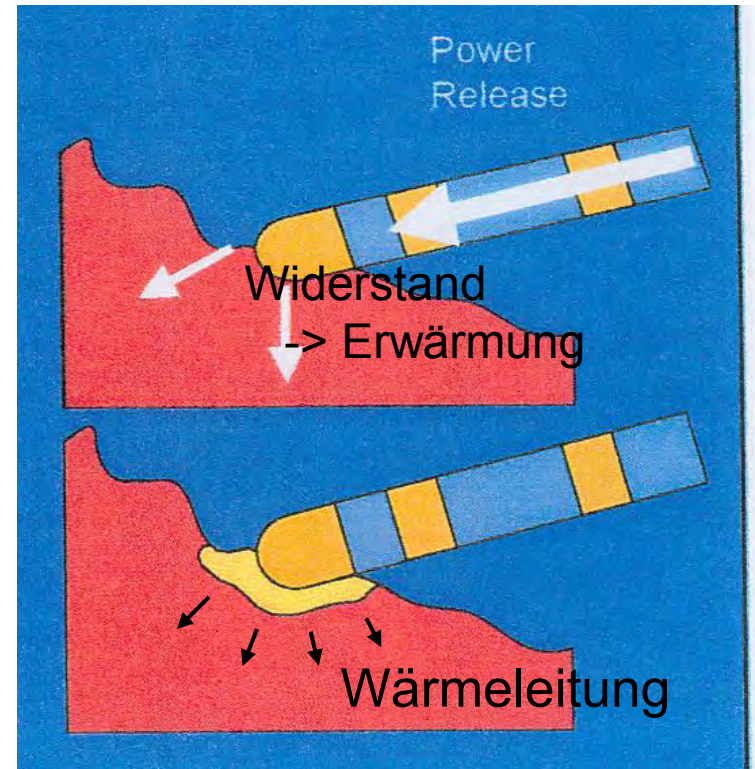
Strom

Spannung

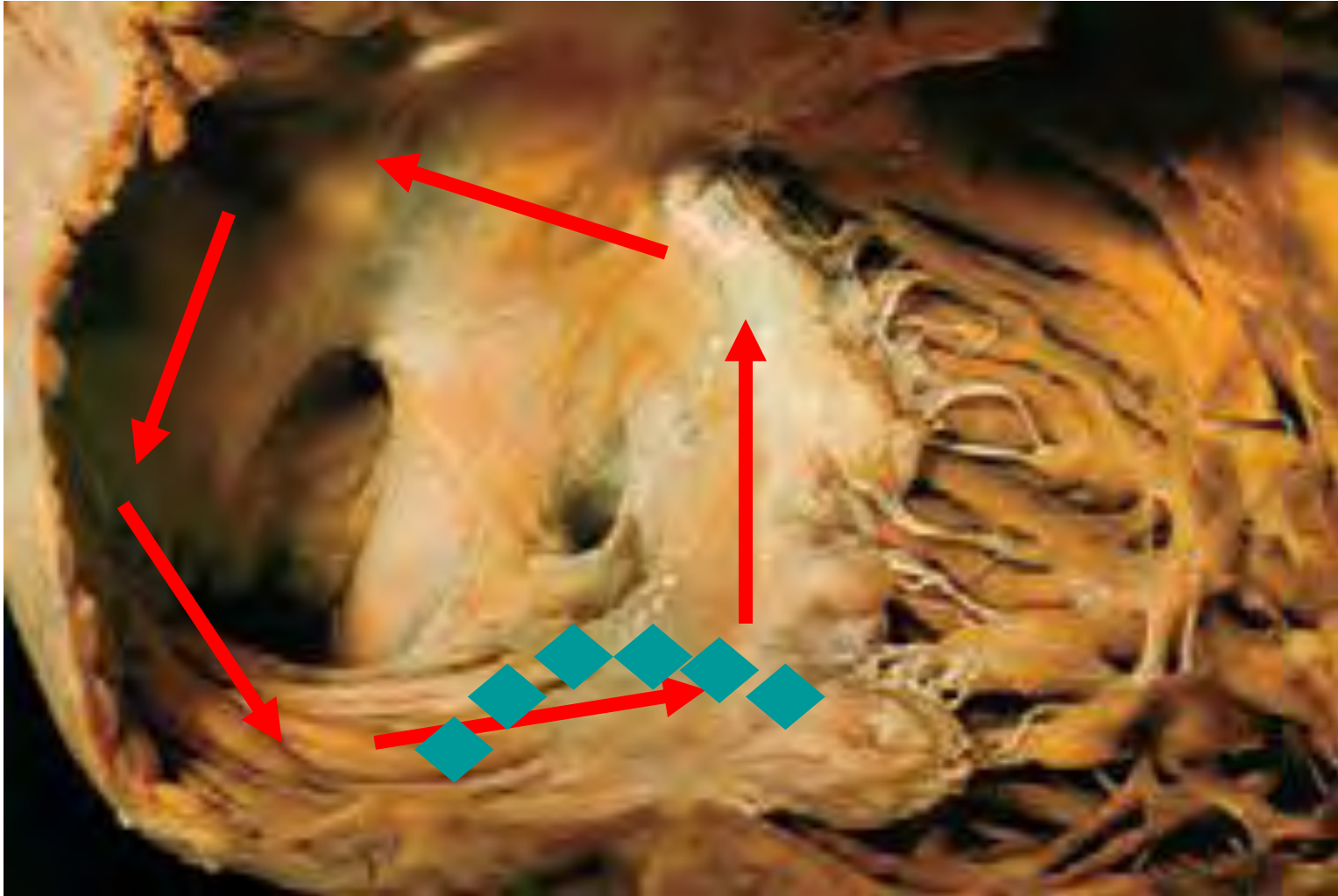
Impedanz („Widerstand“)

Leistung

Unipolar / Bipolar



„Isthmusablation“

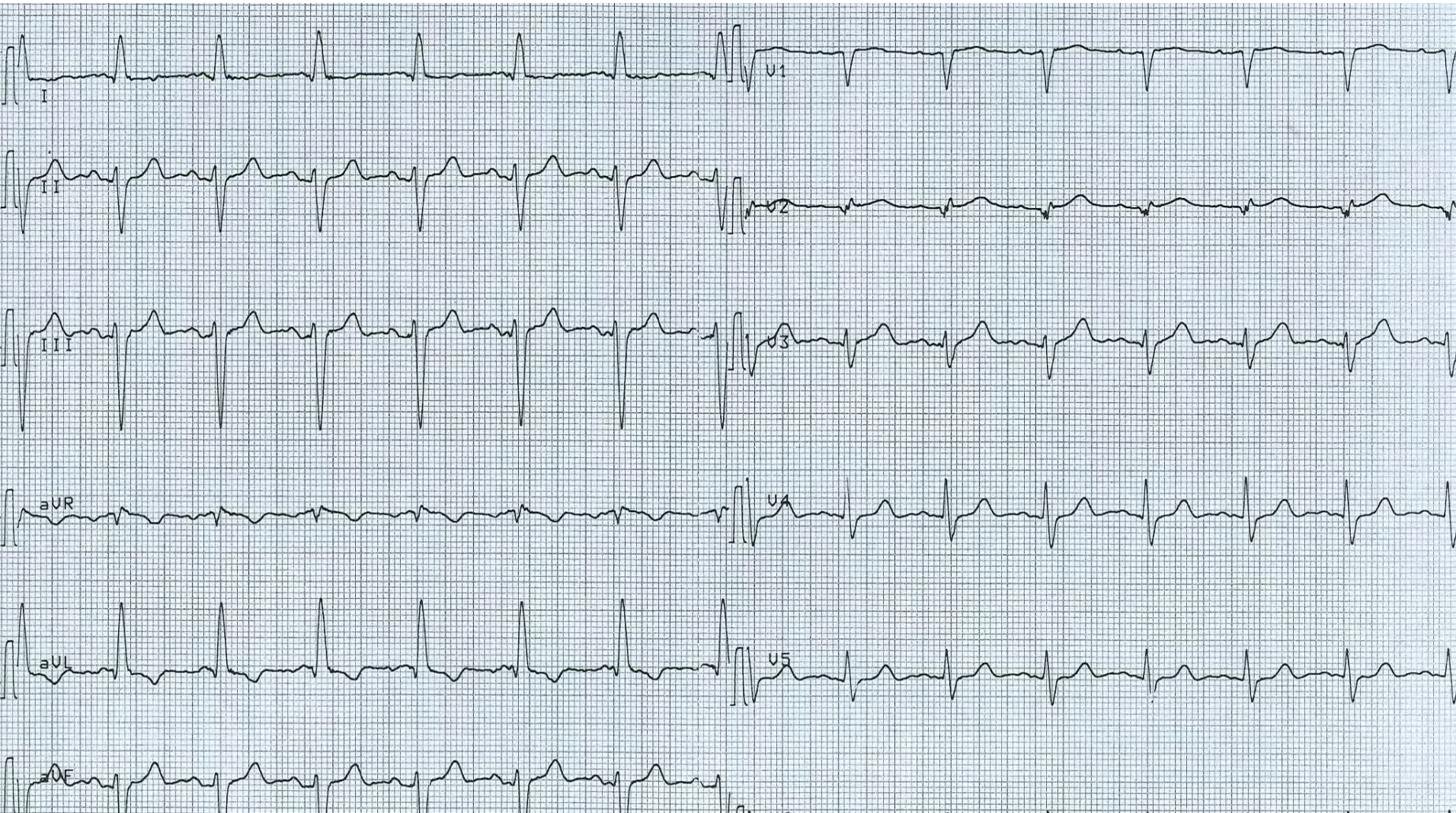


Weltweite Erhebung zur Wirksamkeit und Sicherheit von Katheterablation bei AFib

- **Gesamterfolgsrate 76 %**
- **Von 8745 Patienten:**
 - 27,3 % benötigten nur einen Eingriff
 - 52,0 % waren asymptomatisch ohne medikamentöse Behandlung
 - 23,9 % waren asymptomatisch mit Antiarrhythmika innerhalb <1 Jahres
- **Sehr unterschiedliche Ergebnisse in den verschiedenen Zentren**

Sinusrhythmus nach 3 Monaten

LV Funktion normalisiert nach 3 Monaten



St. n. Vorhofflimmern

St. n. Vorhofflattern (ablatiert)

aktuell (3 Mo): keine Hinweise auf Rezidiv

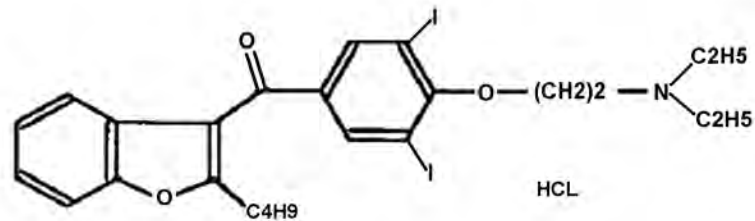
Wie weiter ?

Amiodaron/Antiarrhythmikum weiter?

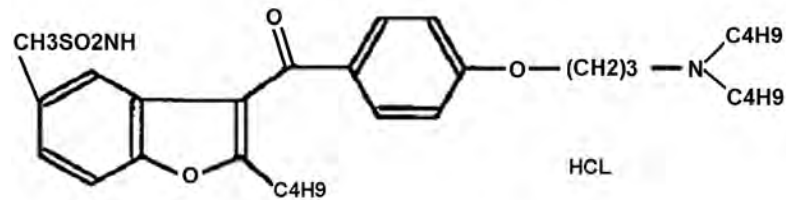
Orale Antikoagulation wie lange ?

Herzinsuffizienztherapie?

Dronedarone vs. Amiodarone



Amiodarone



Dronedarone

St. n. Vorhofflimmern

St. n. Vorhofflattern (ablatiert)

aktuell (3 Mo): keine Hinweise auf Rezidiv

Wie weiter ?

- 24 Stunden EKG (Holter) 3 Monate später unauffällig
- Amiodarone abgesetzt nach 3 Monaten
- OAK wie lange ?
- Herzinsuffizienztherapie je nach Klinik (Ursache behoben)

M. P.

80 j. Patient mit progredienter Dyspnoe seit 8 Monaten
NYHA III (bewegt sich wenig, s.u.), keine Orthopnoe
2x Elektrokonzersion 2002/2003 bei Vorhofflimmern

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Cave:

**Patient/Symptom und keine
„Diagnose“ therapieren:
Herzinsuffizienz**

-> Echokardiographie: diffus eingeschränkte
Kontraktionen LVEF 25%

Gründe für eine schlechte systolische Pumpfunktion ?

PHILIPS

MESSERLI EDI

17/04/2007

13:45:38

TIS0.7

MI 1.4

12/03/1949 27401320070417

S5-1/Adult

FR 42Hz

20cm

2D

60%

C 50

P Low

HGen

M3



JPEG

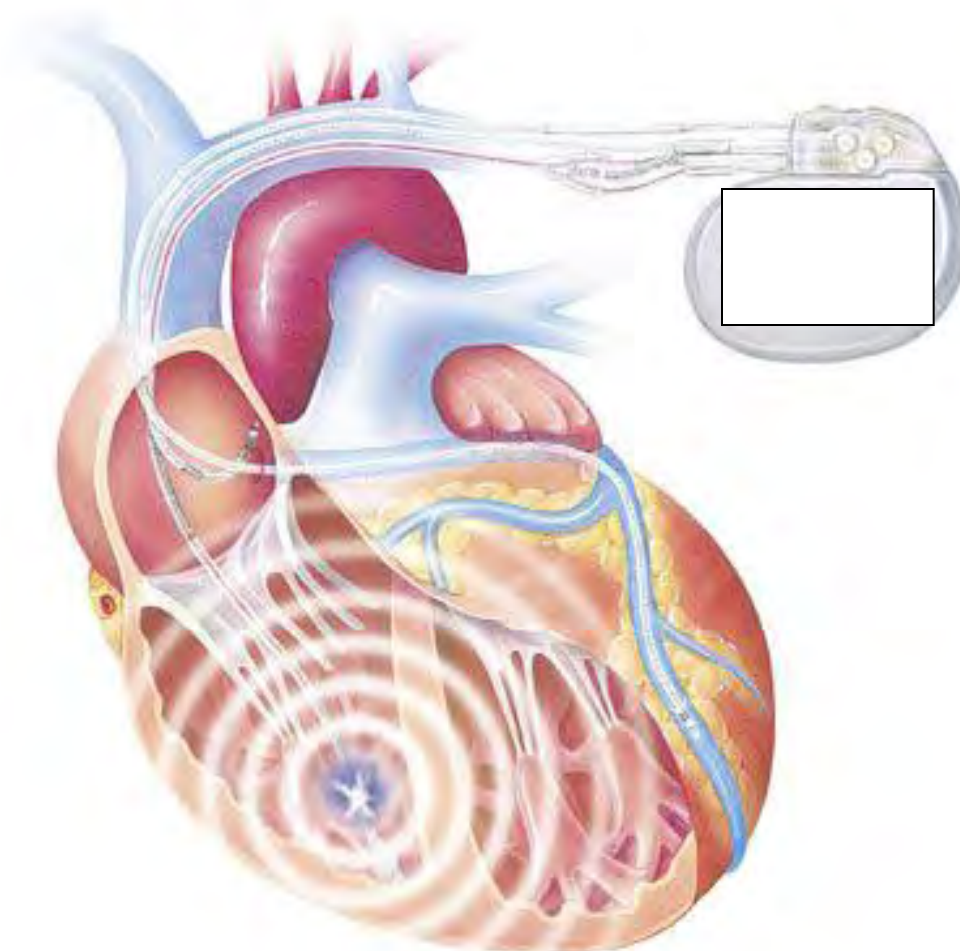
116 bpm

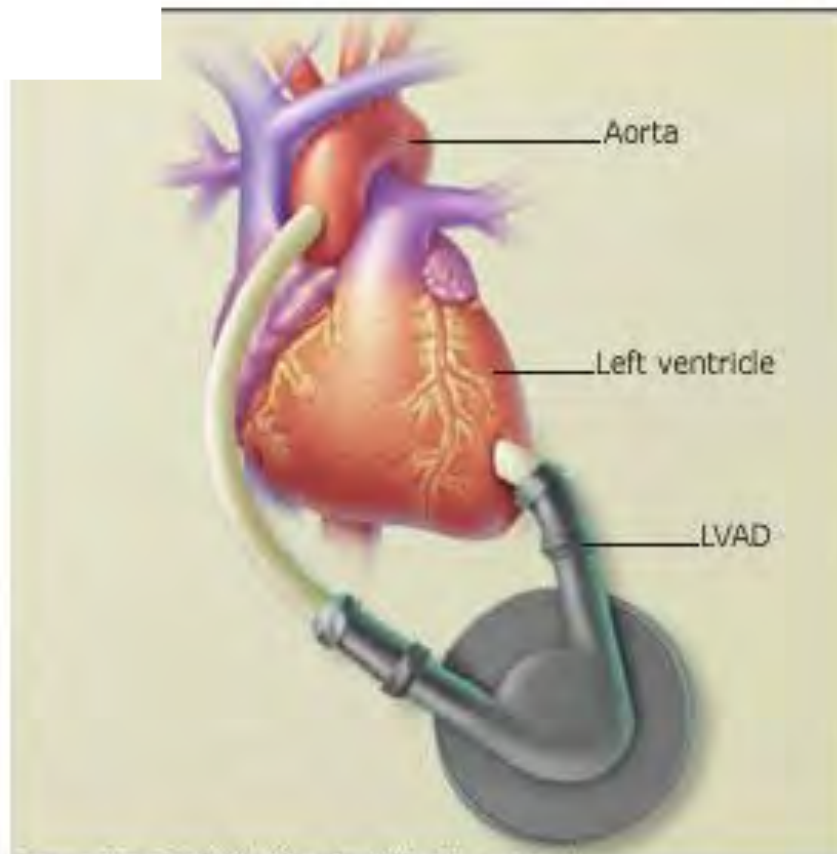
Herzinsuffizienztherapie

Medikamente

- Ursache beheben (u.a. Amiodarone)
- ACE-Hemmer
- AT-II Agonisten
- Betablocker
- Diuretika
- Digitalis (?)

-> nicht-medikamentöse Therapien?





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