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Department of Internal Medicine
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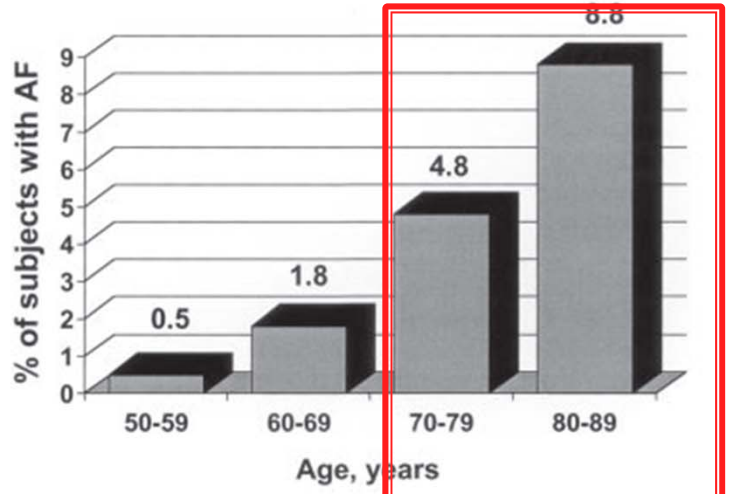
Atrial Fibrillation in Heart Failure, Importance of Age

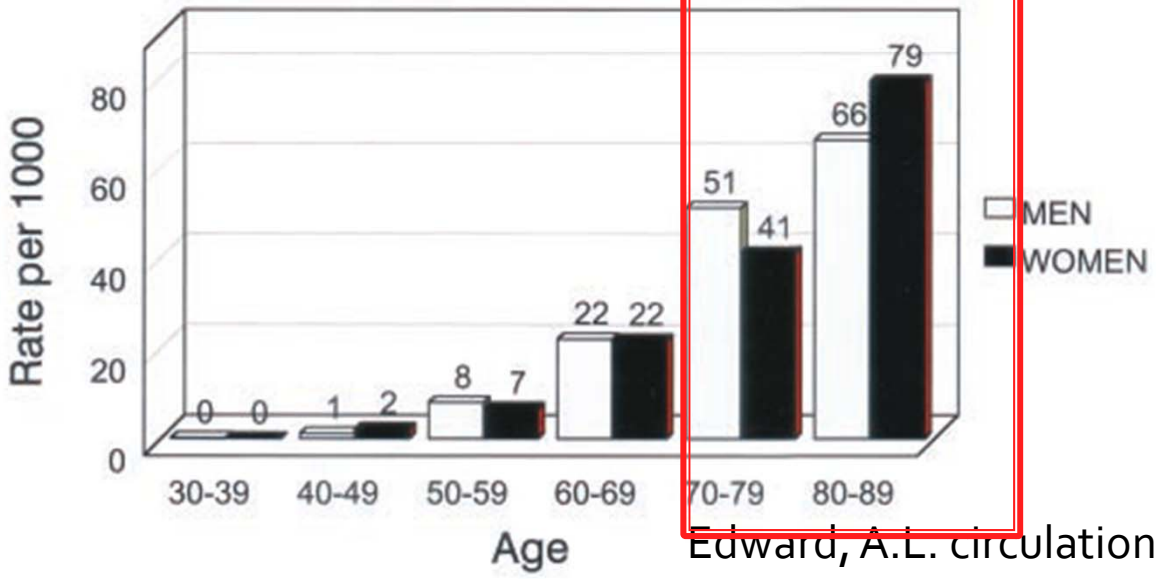
Prevalence of HF and AF in Framingham

AF and HF are two major CV disease in the elderly

AF



Heart failure



Edward, A.L. circulation: 2003:107:139

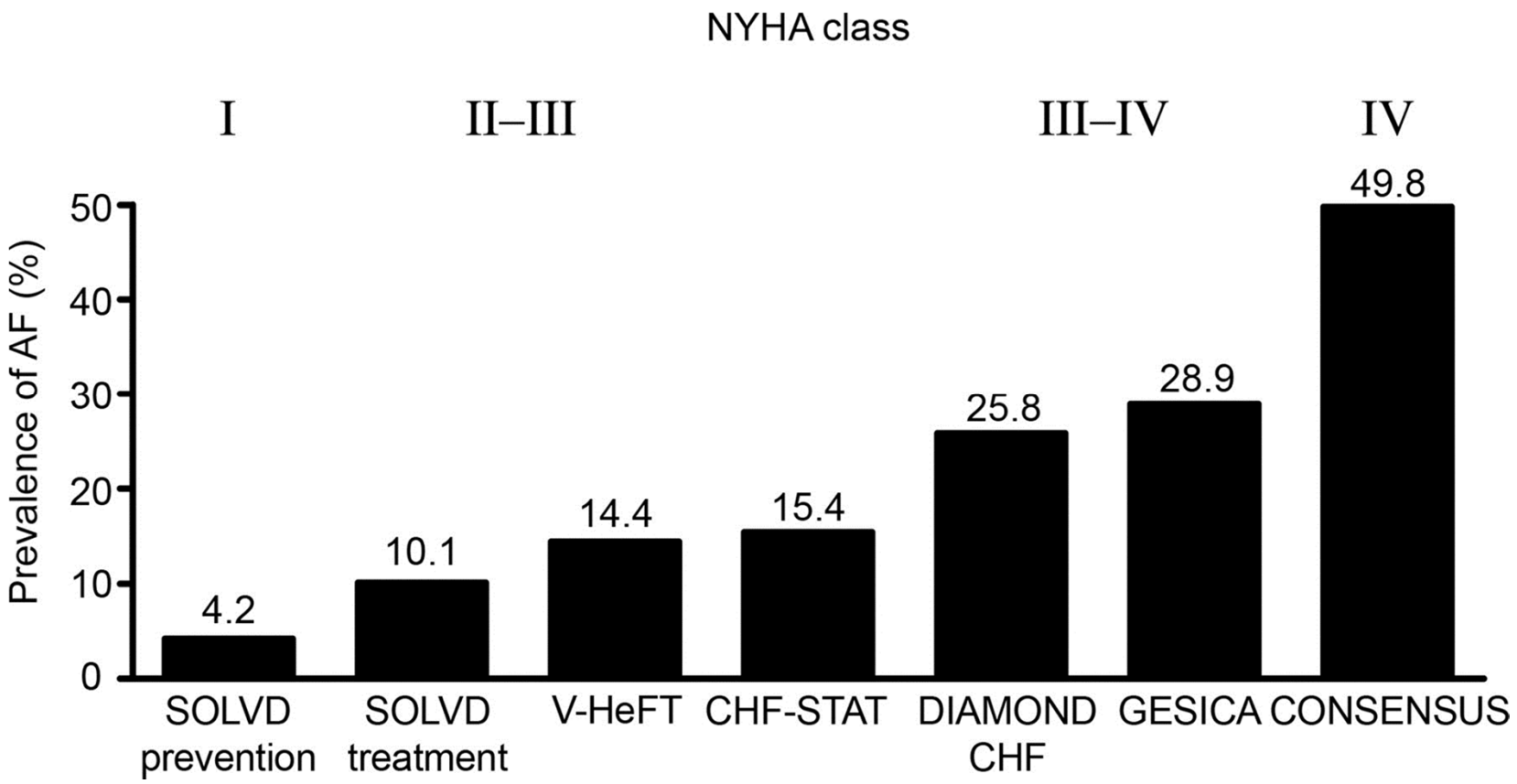
Epidemiology in AF in CHF

- Overall prevalence of AF : 1%
  Elderly people 5% ≥ 65 yr old
  10% ≥ 75 yr old (50% of all AF)

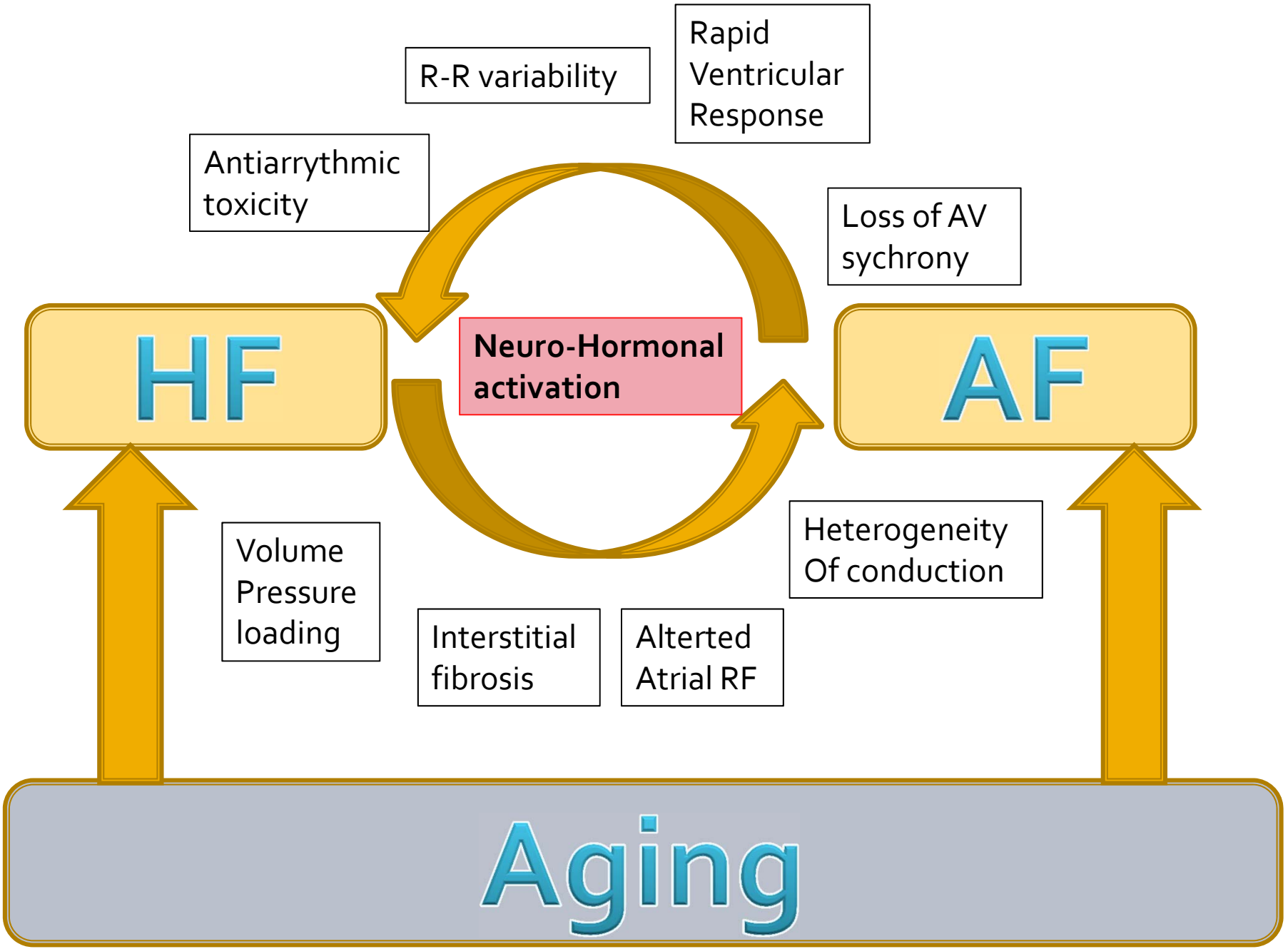
- HF increase a risk of AF :
  HR 4.5 in men and 4.9 in women

- AF is found in 30-40% of HF

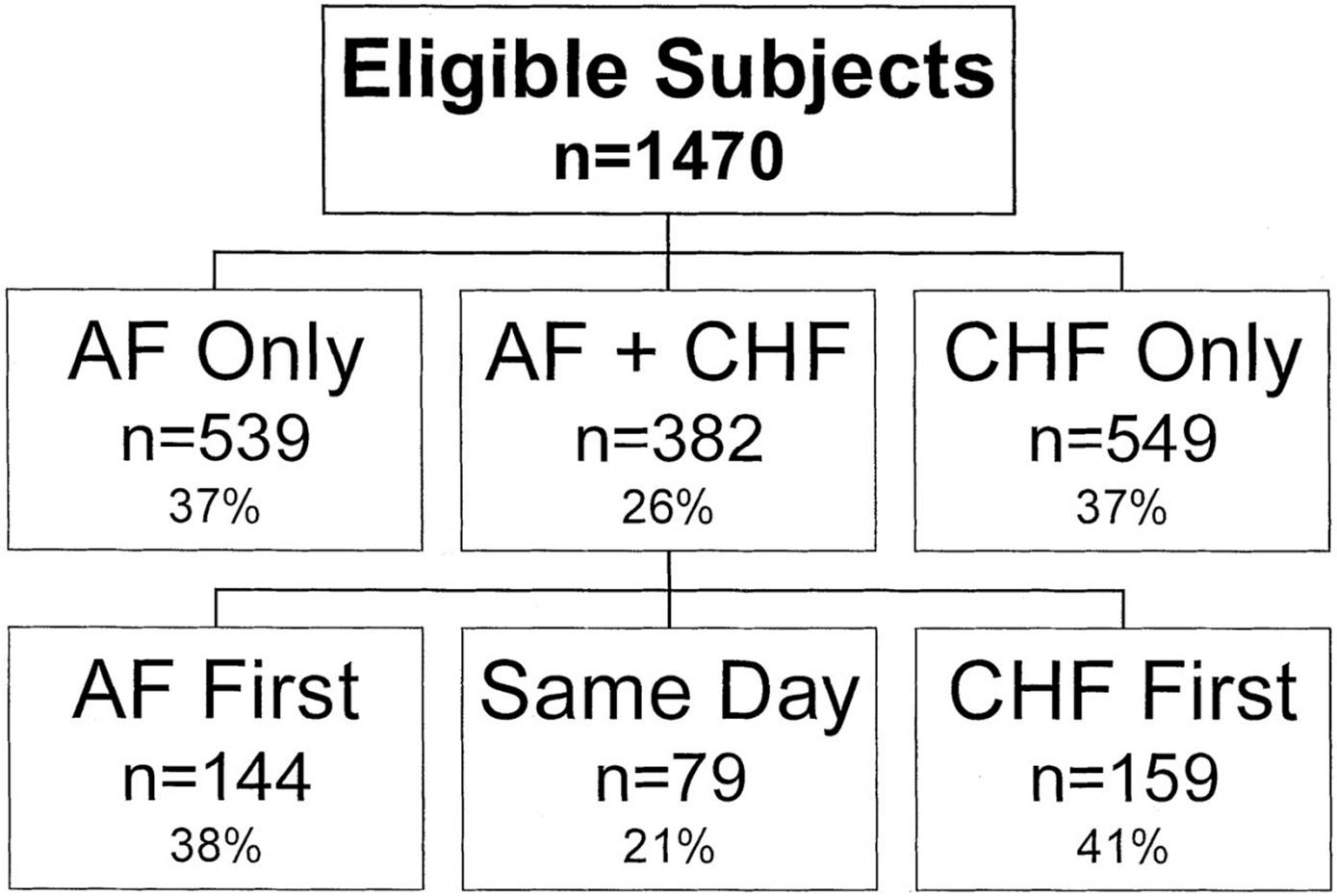
Prevalence of AF is higher in Severe HF



Neuberger H et al. Eur Heart J 2007;28:2568

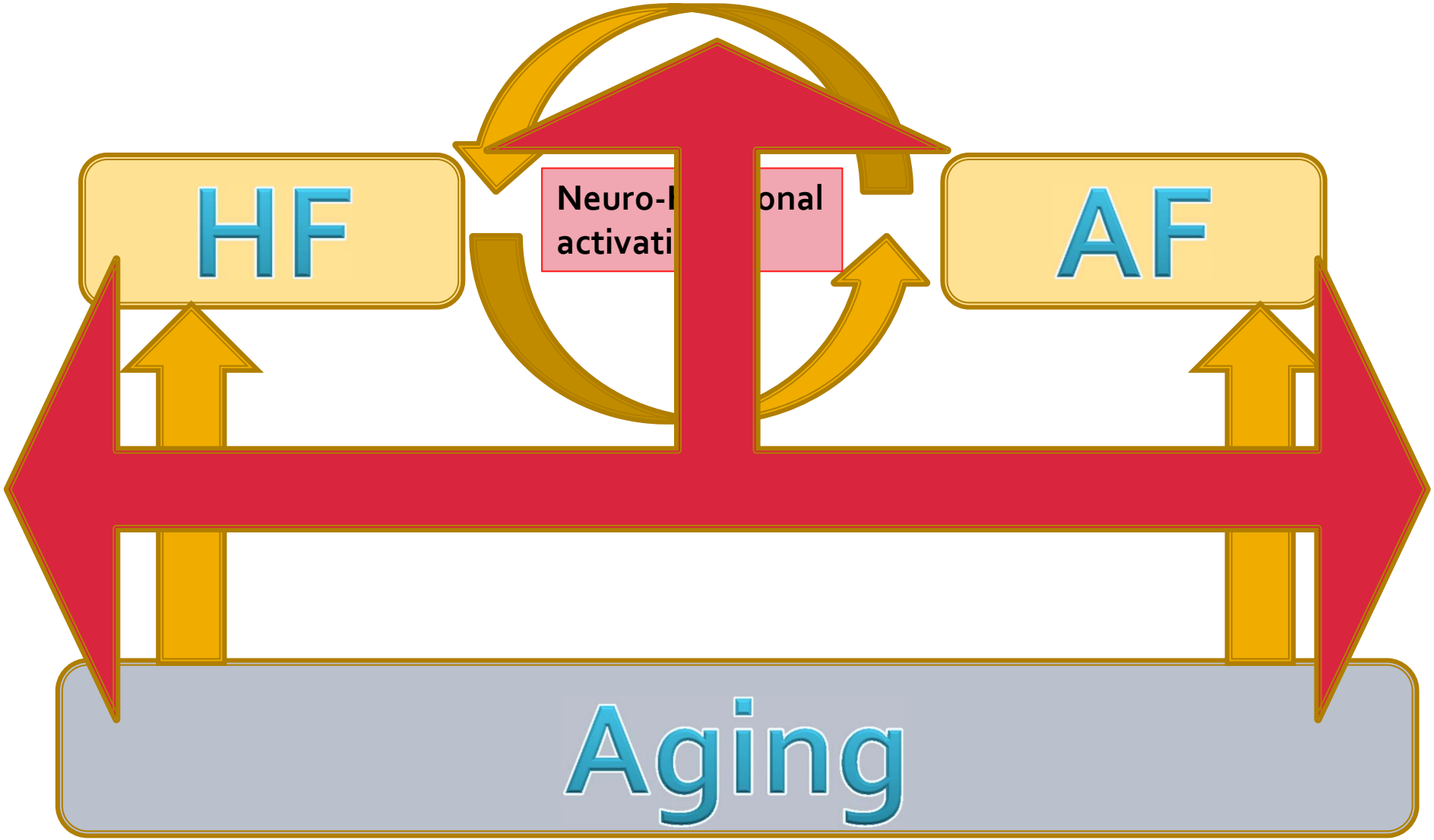

R-R variability
Rapid Ventricular Response
Antiarrythmic toxicity
Loss of AV sychrony
HF
Neuro-Hormonal activation
AF
Volume Pressure loading
Heterogeneity Of conduction
Interstitial fibrosis
Alterted Atrial RF
Aging

AF Preceded CHF about as often as CHF preceded AF: common pathophysiologic substrate



Wang, T. J. et al. Circulation 2003;107:2920-2925

Upstream Tx: ACEi or ARB, BB
Aldosteron antagonist, statin, PUFA



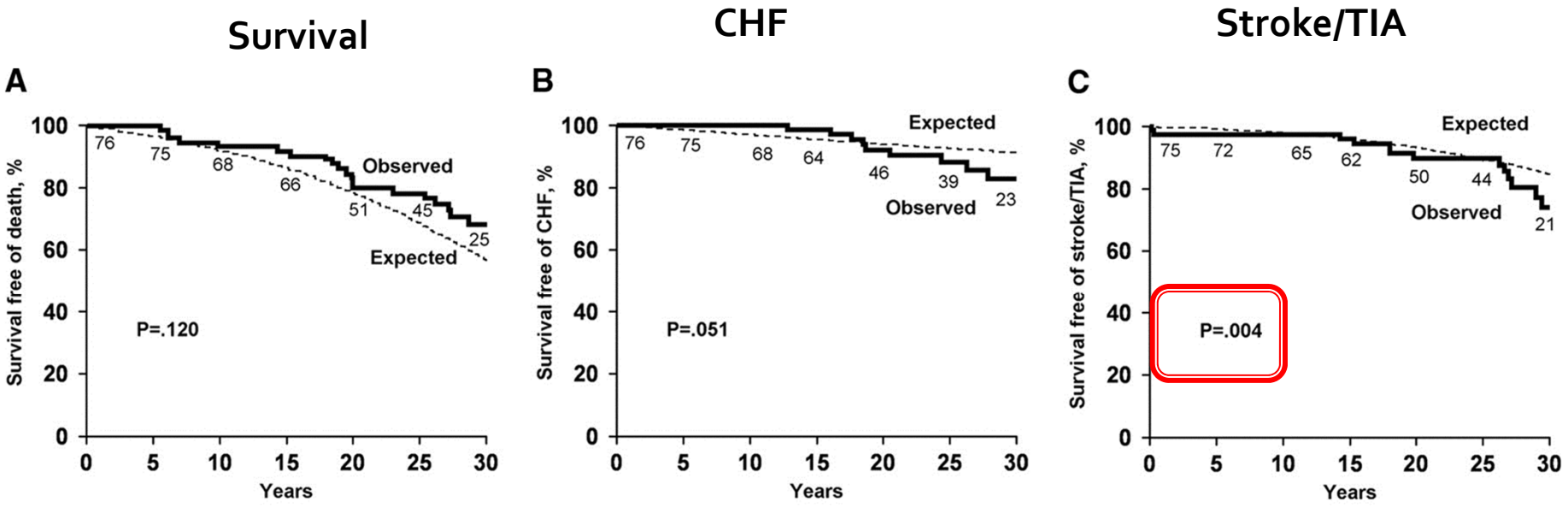
Is different treatment of AF in CHF in Elderly?

Occurrence of AF and HF in aging

Lone AF

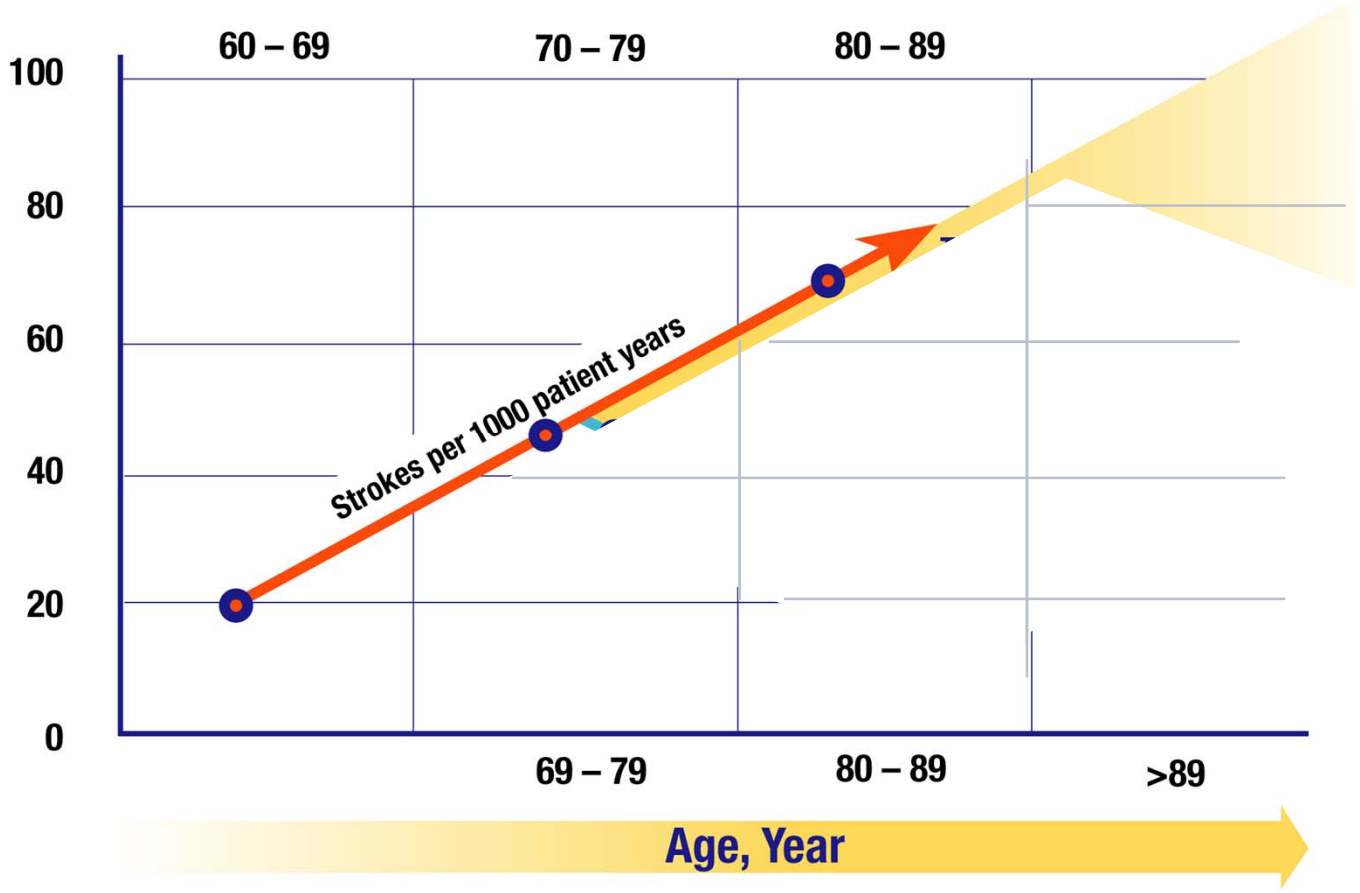
Long-term progression and outcome with aging in lone AF

76 patients with lone AF diagnosed in 1950~1980
25.2±9.5 year follow up



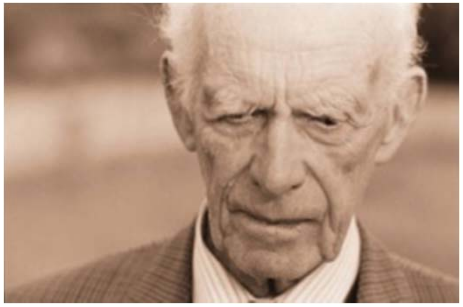
Circulation. 2007;115:3050-3056

Risk of Stroke is increased with age in AF

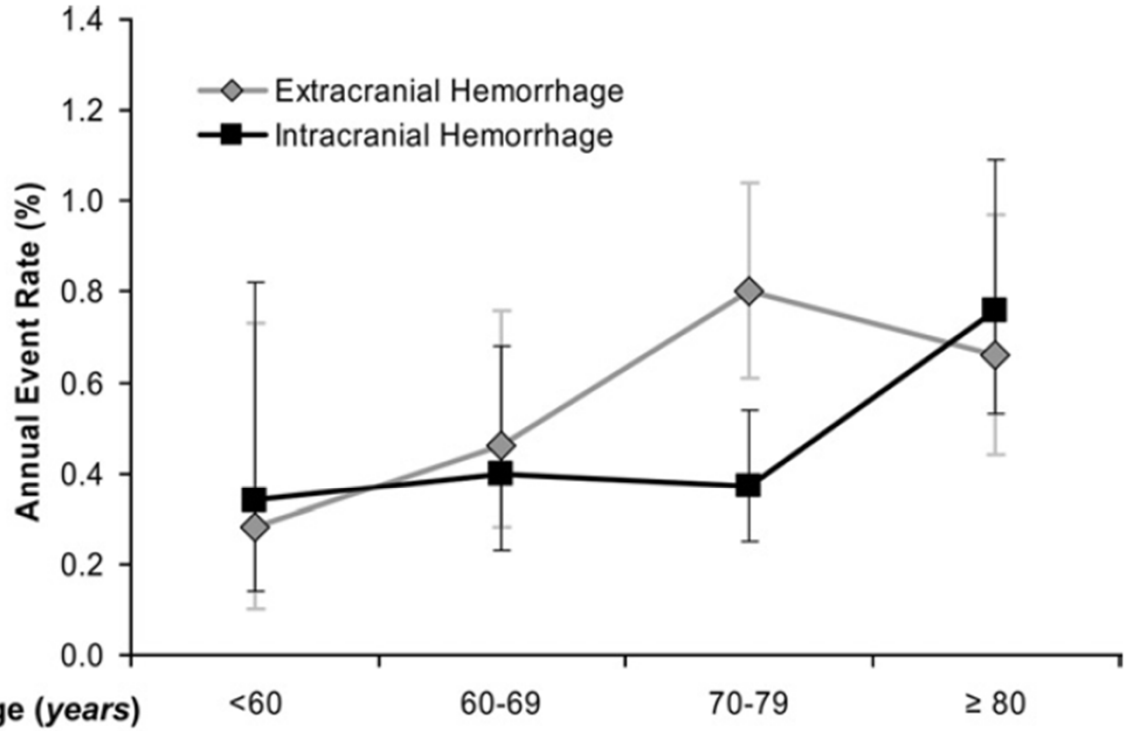


Wolf PA, et al. *Arch Intern Med.* 1987;147:1561-1564.
White R, et al. *Am J Med*. 1999;106:165-171

Aspirin or Warfarin in Elderly-AF



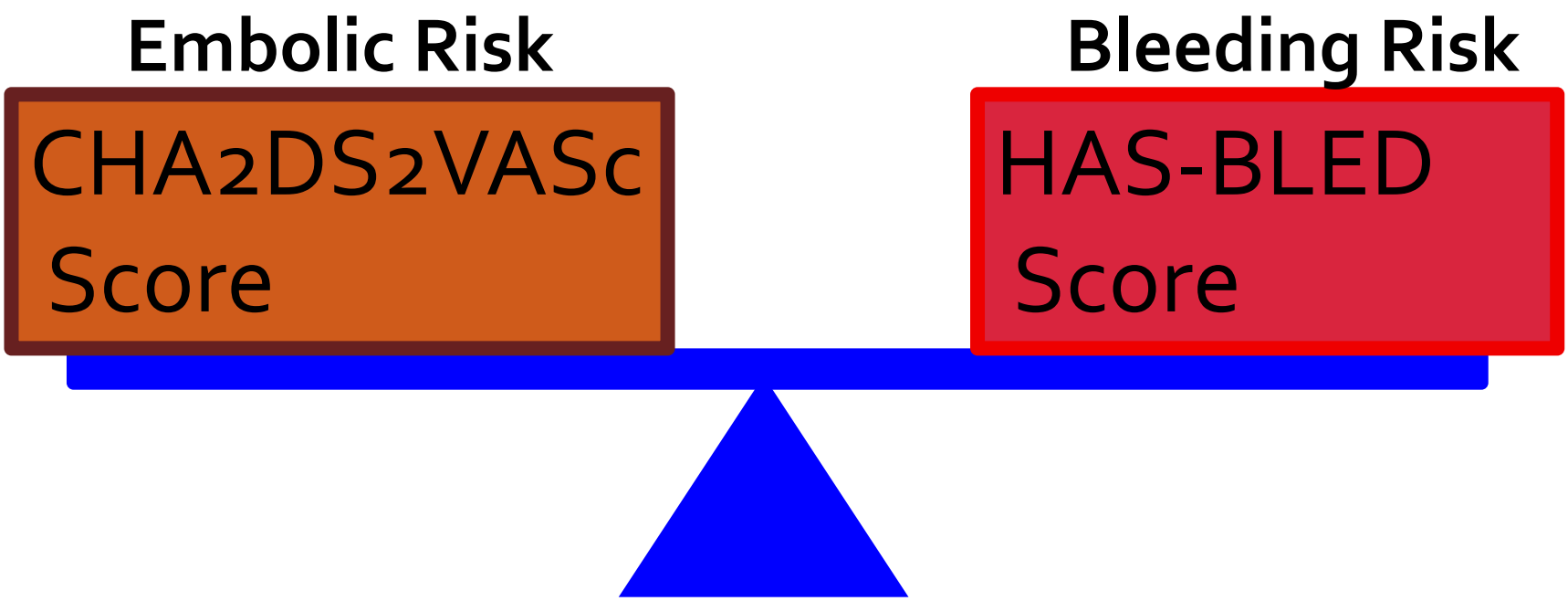
Age and the risk of warfarin associated hemorrhage: ATRIA Study



Age (*years*)	<60	60-69	70-79	≥ 80
Extracranial				
No. of events	4	15	54	25
Rate [95%CI]	0.28 [0.10-0.73]	0.46 [0.28-0.76]	0.80 [0.61-1.0]	0.66 [0.44-0.97]
Intracranial				
No. of events	5	13	25	29
Rate [95%CI]	0.34 [0.14-0.82]	0.40 [0.23-0.68]	0.37 [0.25-0.54]	0.76 [0.53-1.1]

Fang MC , *J Am Geriatr Soc. 2006;54:1231*

Embolic Risk and Bleeding Risk



$CHADS_2$ → CHA_2DS_2VASc

CHADS2 Risk	Score
CHF	1
Hypertension	1
Age > 75	**1**
Diabetes	1
Stroke or TIA	2

CHA2DS2-VASc Risk	Score
CHF or LVEF ≤ 40%	1
Hypertension	1
Age ≥ 75	**2**
Diabetes	1
Stroke/TIA/ Thromboembolism	2
Vascular Disease	1
Age 65 - 74	**1**
Female	1

2010 ESC AF guideline

Approaches to thromboprophylaxis in AF

CHA2DS2-VASc Score	Recommended Antithrombotic tx.
≥2	**Warfarin**
1	Either anticoagulation or aspirin **Preferred warfarin**
0	Either aspirin or no antithrombotic **Preferred no antithrombotic**

2010 ESC AF guideline

Use of warfarin in AF by Age in 2010 ESC guideline

≥75 yr	• warfarin
65-75 yr	• Other risk +1: **warfarin** • No minor risk: prefer **warfarin** than ASA

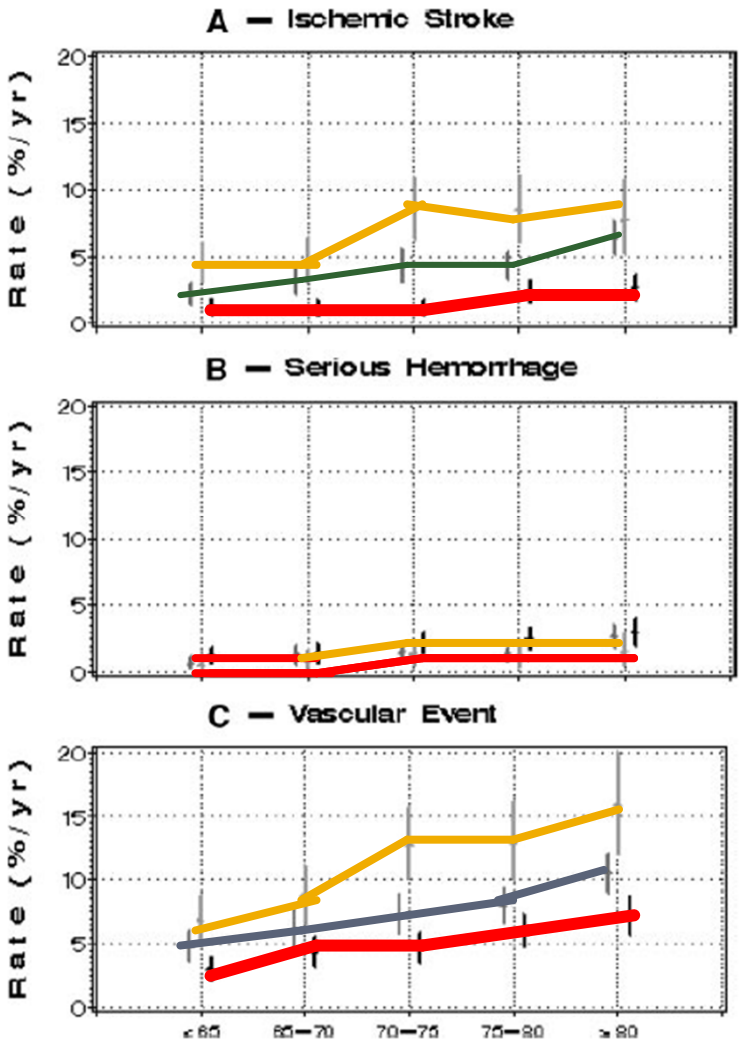
2010 ESC AF guideline

Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA)

- 973 patients ≥ 75 yrs with AF assigned to warfarin (INR 2–3) vs aspirin (75 mg/day)
- Primary endpoint – fatal or disabling stroke, ICH or systemic embolism
  - Risk per year
    - Warfarin: **1.8%;** Aspirin: **3.8%**
    - Relative risk warfarin vs aspirin: **0.48; *P* = 0.003**
- Major extracranial hemorrhage
  - Risk per year
    - Warfarin: 1.4%; Aspirin: 1.6%
    - Relative risk warfarin vs aspirin: **0.87**

Mant J, et al. *Lancet*. 2007;370:493-503.

Net clinical benefit for warfarin vs. antiplatelet (meta-analysis of 12 RCT)



Control

Anti-platelet

warfarin

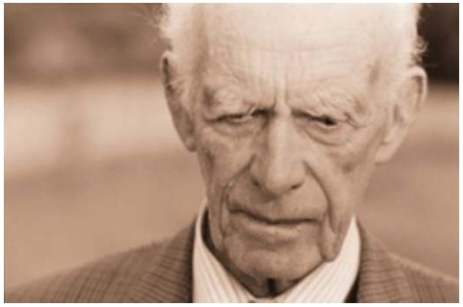
van Walraven, C. Stroke 2009;40: 1410-1416

HAS-BLED Bleeding Risk Score

A score ≥3 high risk and some caution and regular review

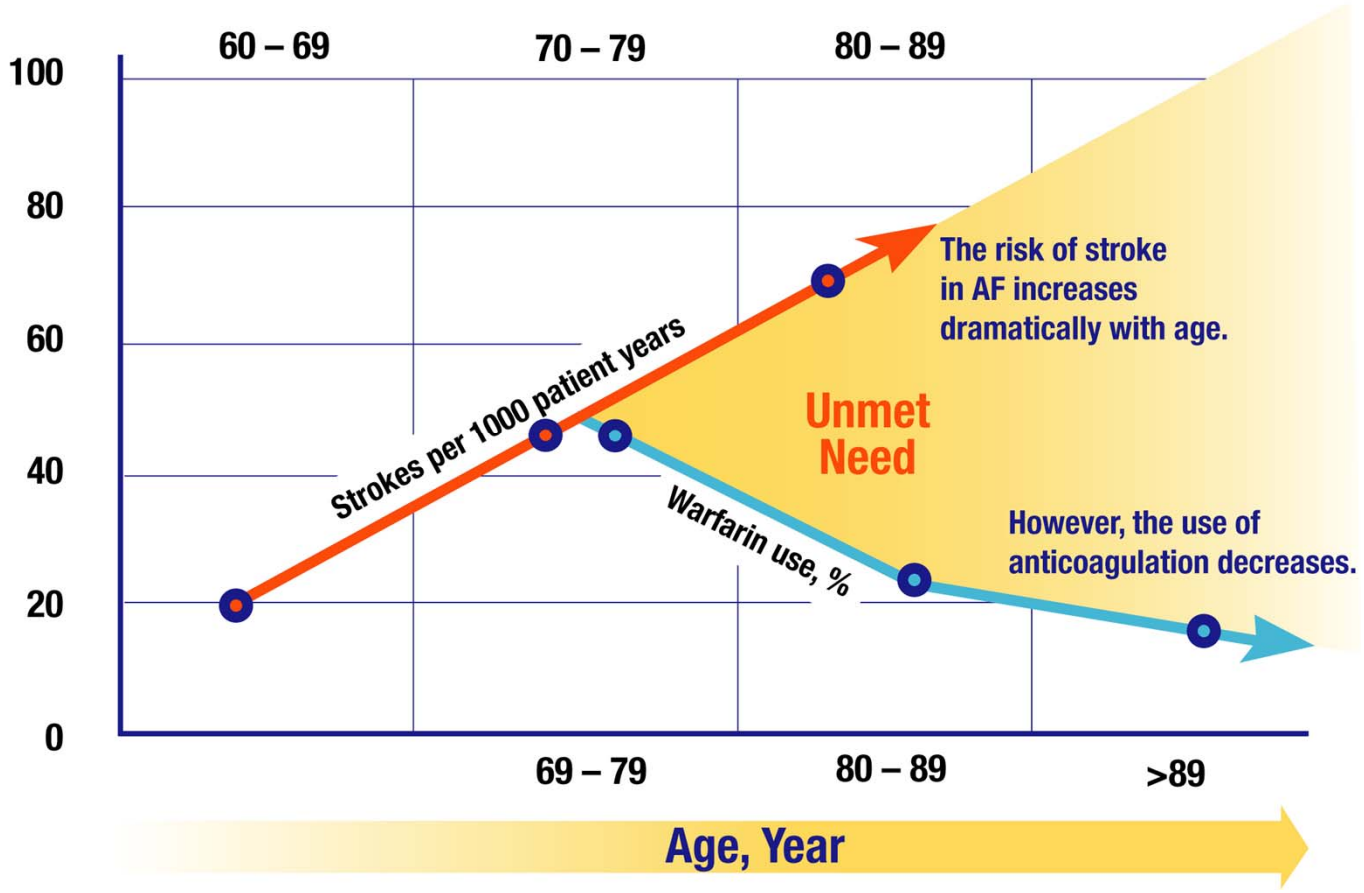
Letter	Clinical Characteristics	Explanation	Point
H	Hypertension	SBP≥160	1
A	Abnormal Renal and liver Disease(1 point each)	Cr≥2.2 mg/dl Liver cirrhosis or bilirubin> 2×ULN or AST/ALT/ALP> 3×ULN	1 or 2
S	Stroke		1
B	Bleeding	Bleeding Hx or diasthesis	1
L	**Labile INRs**	**TTR< 60%**	**1**
E	**Elderly(>65)**		1
D	Drug or Alcohol (1 point each)	Drug: NSAIDs, antiplatelet	1 or 2
			Maximum 9

Aspirin or Warfarin in Elderly



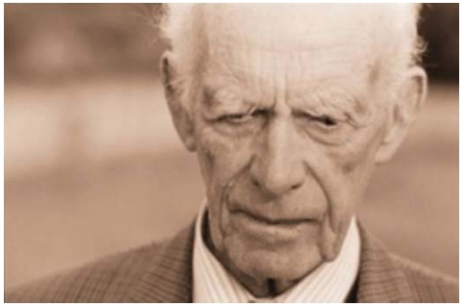
- Efficacy — more effective
- Safety — slightly less major hemorrhage
- Practice — possible but difficult

Age-Related Trends in Atrial Fibrillation: A Focus on Risk of Stroke



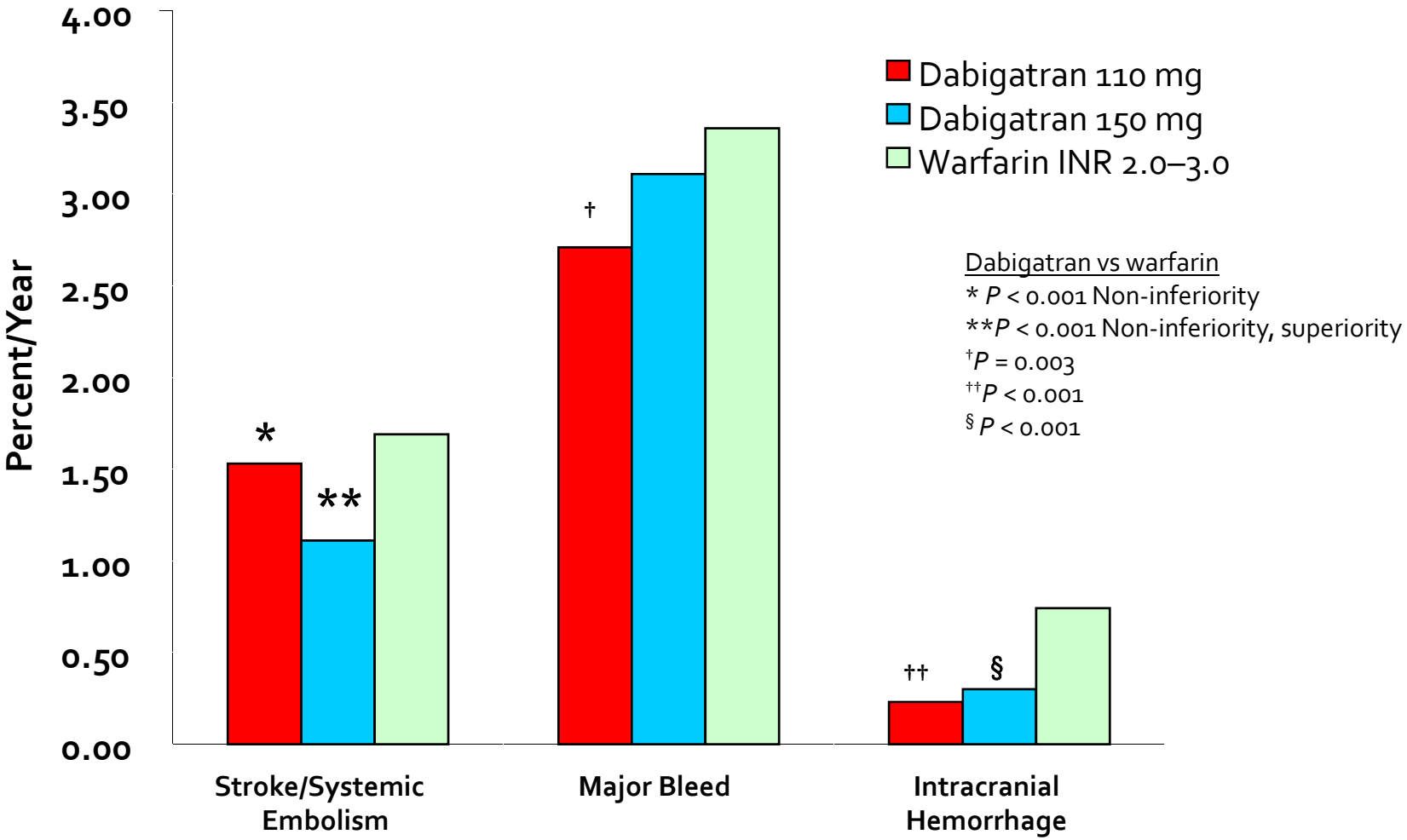
Wolf PA, et al. *Arch Intern Med.* 1987;147:1561-1564.
White R, et al. *Am J Med*. 1999;106:165-171

~~Aspirin or Warfarin in Elderly~~



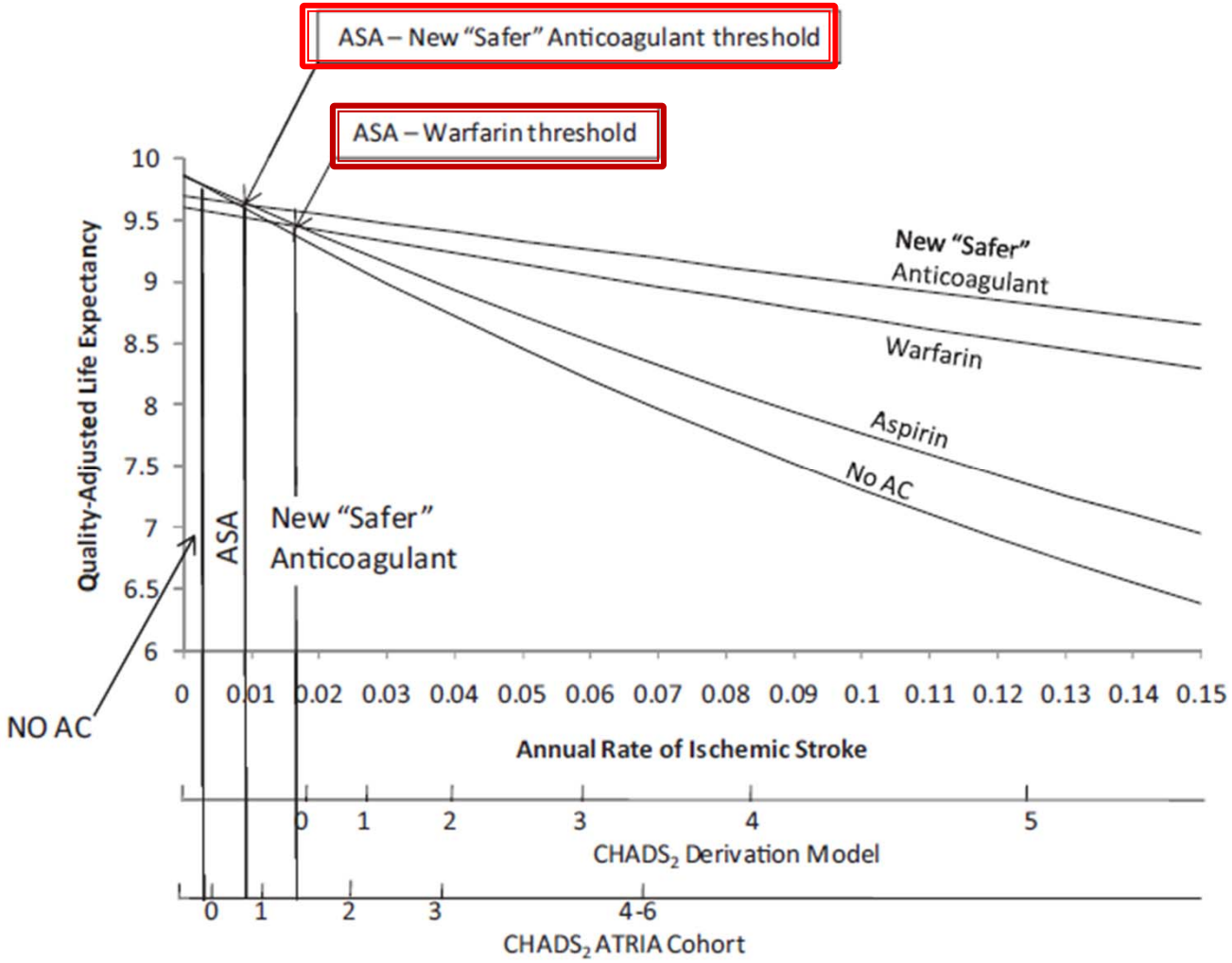
- **We need more effective and safe drug without monitoring**

Stroke Prevention in Atrial Fibrillation
Dabigatran etexilate vs warfarin (RE-LY)



Connolly S, et al. *N Engl J Med*. 2009;361:1139-1151.

New Safer anticoagulaton threshold may be lowered



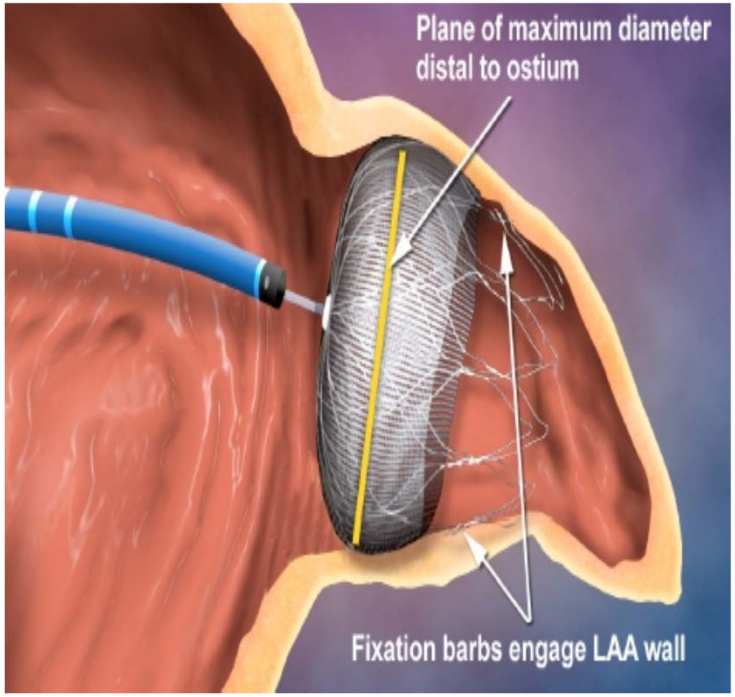
Circ Cardiovasc Qual Outcomes. **2011;4:14-21**

New Approaches to thromboprophylaxis in AF

CHA2DS2-VASc Score	Recommended Dabigatran
≥2	Has-BLED Score ▪ 0-2 dabigatran 150 mg bid ▪ ≥ 3 dabigatran 110 mg bid
1	Consider Dabigatran 110 mg than warfarin or aspirin
0	Either aspirin or no antithrombotic **Preferred no antithrombotic**

2010 ESC AF guideline

Left Atrial Appendage (LAA) Closure vs Warfarin for Prevention of Stroke in Patients with AF



Efficacy

Composite endpoint of stroke, cardiovascular death, and systemic embolism

- Intervention: **3.0** events per 100 patient yrs
- Warfarin Control: **4.9** events per 100 patient yrs
- Rate ratio (95% CI): **0.62** (0.35–1.25)
- Intervention probability of non-inferiority > 99.9%

Safety

Composite endpoint of events related to excessive bleeding or procedure-related complications

- Intervention: **7.4** events per 100 patient years
- Warfarin Control: **4.4** events per 100 patient years
- Rate ratio (95% CI): **1.69**

Holmes D, et al. *Lancet*. 2009;374:534-542.

Occurrence of AF and HF in aging

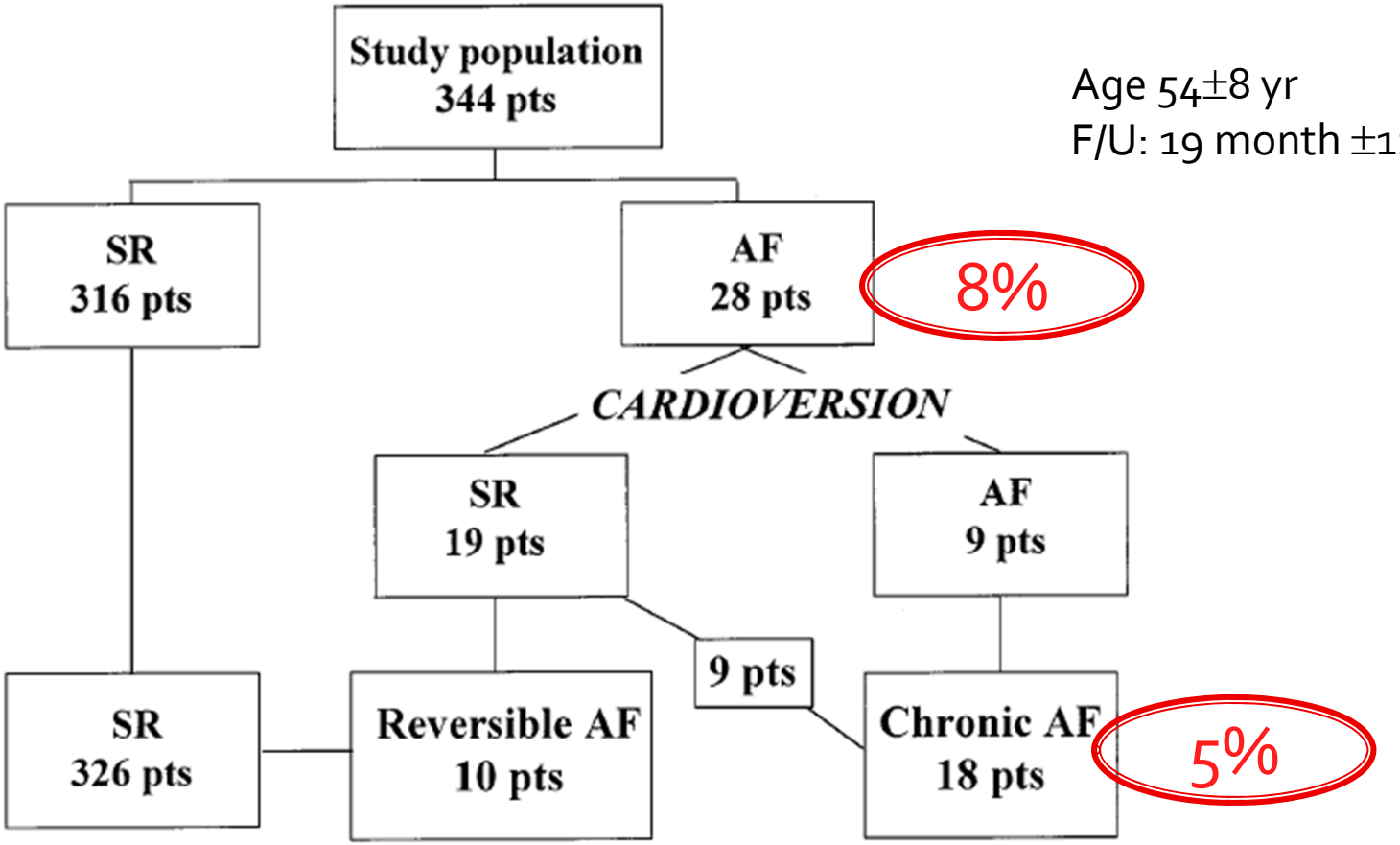
Lone AF

CHF

CHF

AF

When CHF with SR progress to AF

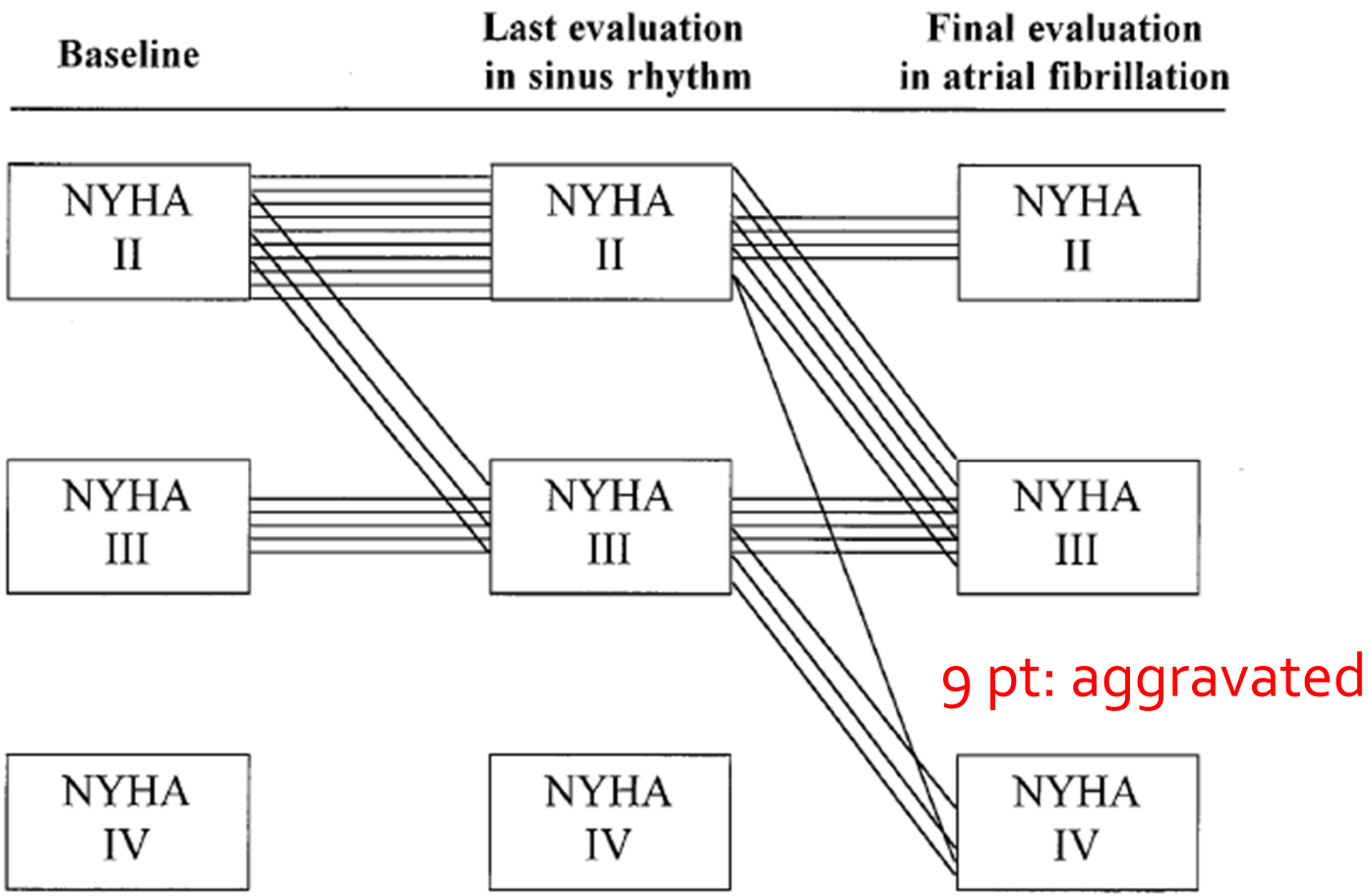


Age 54±8 yr
F/U: 19 month ±12

Pozzoli, M., J Am Coll Cardiol 1998;32:197–204

CHF with SR to AF

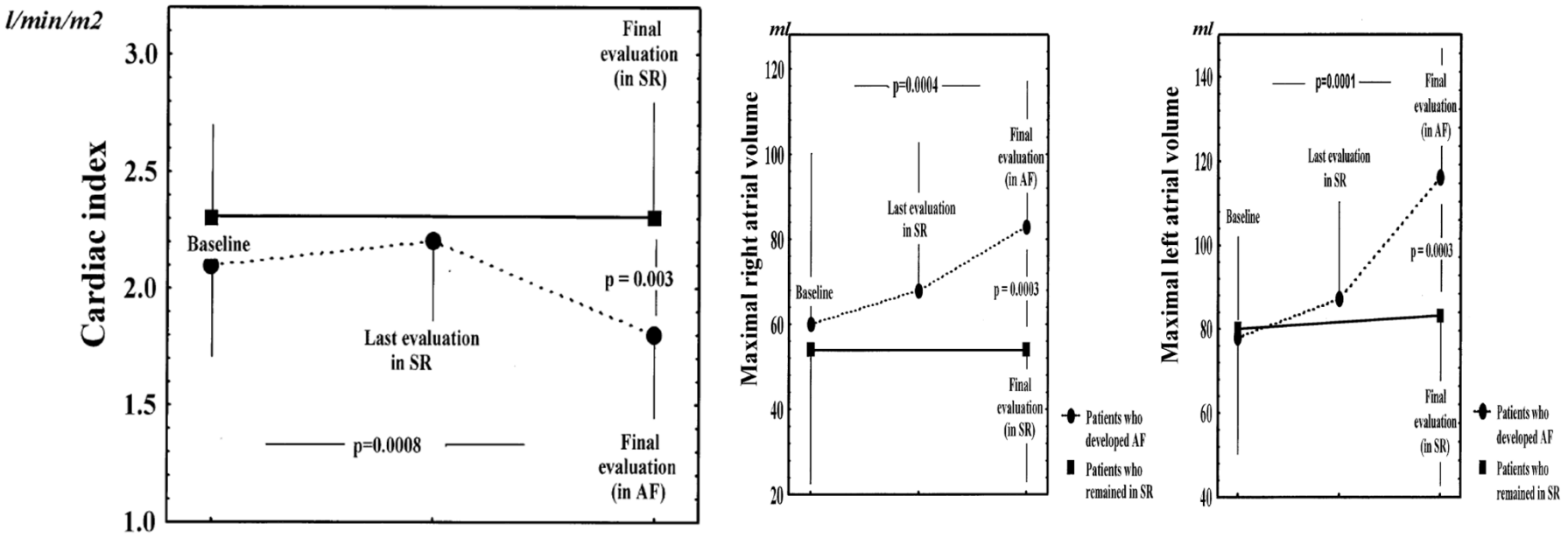
NYHA in 18 pt who developed chronic AF before and after the onset of AF



9 pt: aggravated

Pozzoli, M., J Am Coll Cardiol 1998;32:197–204

CHF with SR to AF



- **Systemic thromboembolism occurred in 3 of the 18 patients with AF.**
- **Nine of 18 patients died after AF**

Pozzoli, M., J Am Coll Cardiol 1998;32:197–204

Occurrence of AF and HF in aging

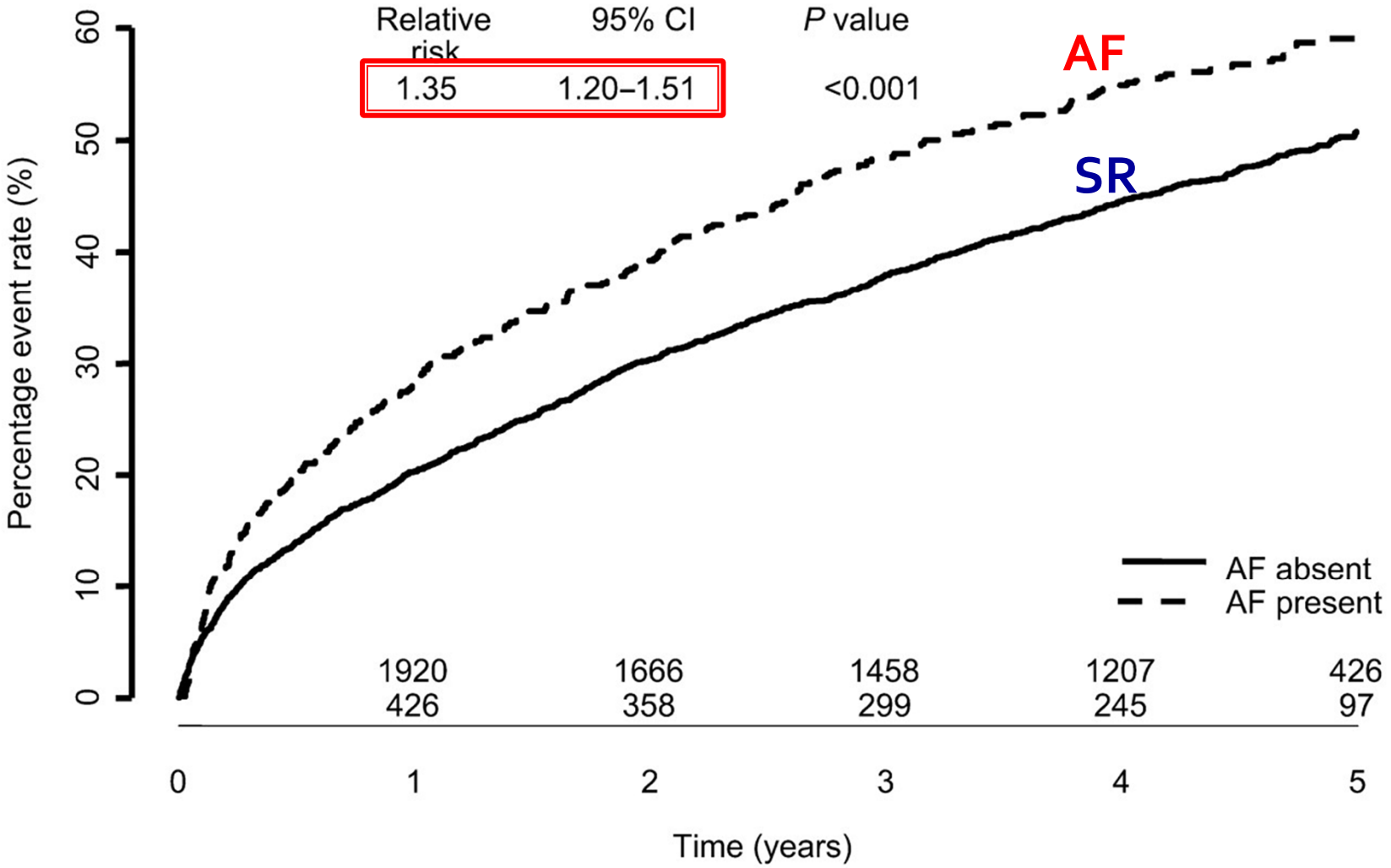
1. Lone AF
   - CHF
2. CHF
   - AF
3. CHF
   - Permanent AF

Prognostic relevance of atrial fibrillation from COMET

Multivariable analysis of risk of all-cause mortality in patients with AF vs. No AF at baseline

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 41–120 vs. ≤40 mg	1.366	1.183, 1.578	<0.001
Diuretic dose >120 vs. ≤40 mg	1.633	1.374, 1.939	<0.001
AF vs. No AF	1.069	0.921, 1.242	0.3811

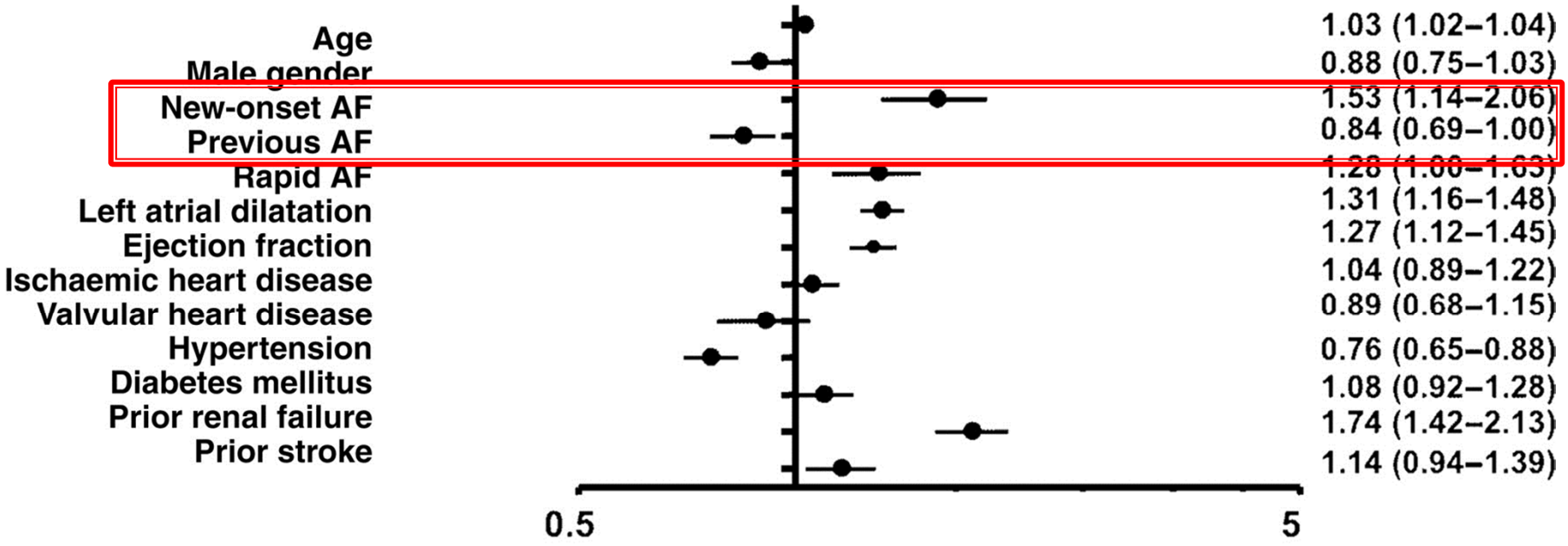
Mortality following new onset AF in patients with sin us rhythm at baseline form COMETs



Swedberg K et al. Eur Heart J 2005;26:1303-1308

New-onset AF is an independent predictor of in-hospital mortality in hospitalized heart failure patients: results of the EuroHeart Failure Survey

Independent predictors of in-hospital mortality.



*No AF used as reference group.

Rivero-Ayerza M et al. Eur Heart J 2008;29:1618-1624

Meta-analysis of Mortality in CHF patients in sinus rhythm and AF.

AF in CHF Increased mortality OR 1.4

Cohort/subgroup	Mortality		Odds ratio (95% CI)	P-value
	AF	SR		
Randomized trials	1906/4141 (46.0%)	8550/26 107 (32.7%)	1.39 (1.17–1.66)	<0.0001
Randomized trials (adjusted)	1831/3935 (46.5%)	8070/24 886 (32.4%)	1.40 (1.32–1.48)	<0.0001
Randomized trials impaired LV function	1414/2797 (50.5%)	5955/16 640 (35.8%)	1.38 (1.15–1.65)	<0.01
Observational studies	1427/6869 (20.7%)	3834/16 582 (23.1%)	1.52 (1.24–1.86)	<0.0001
Observational studies (adjusted)	1344/6671 (20.1%)	3663/16 036 (22.9%)	1.14 (1.03–1.26)	<0.05
Observational studies impaired LV function	723/1464 (49.3%)	2155/5340 (40%)	1.49 (1.32–68)	<0.0001
Randomized and observational preserved LV function	415/1174 (35.3%)	1493/7347 (20.3%)	2.0 (1.7–2.3)	<0.0001

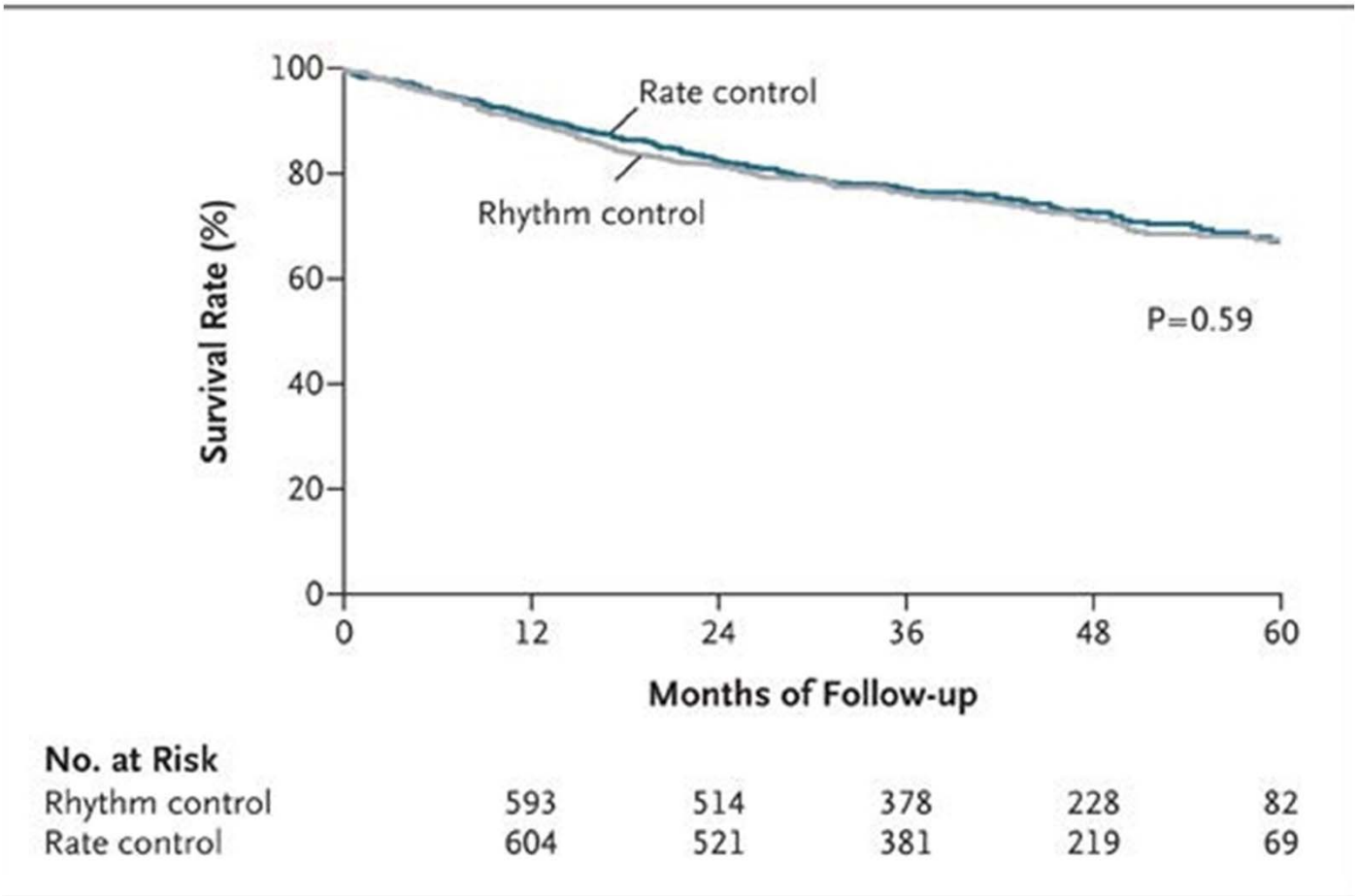
Mamas M A et al. Eur J Heart Fail 2009;11:676-683

Dose AF increase mortality in HF?

- New- onset- AF might aggravate HF and affect the mortality
- Permanent –AF is related largely to comorbid state in the patients group.
- Whether AF itself may affect mortality or AF may be a marker of frailty is in controversy.

AF-CHF study

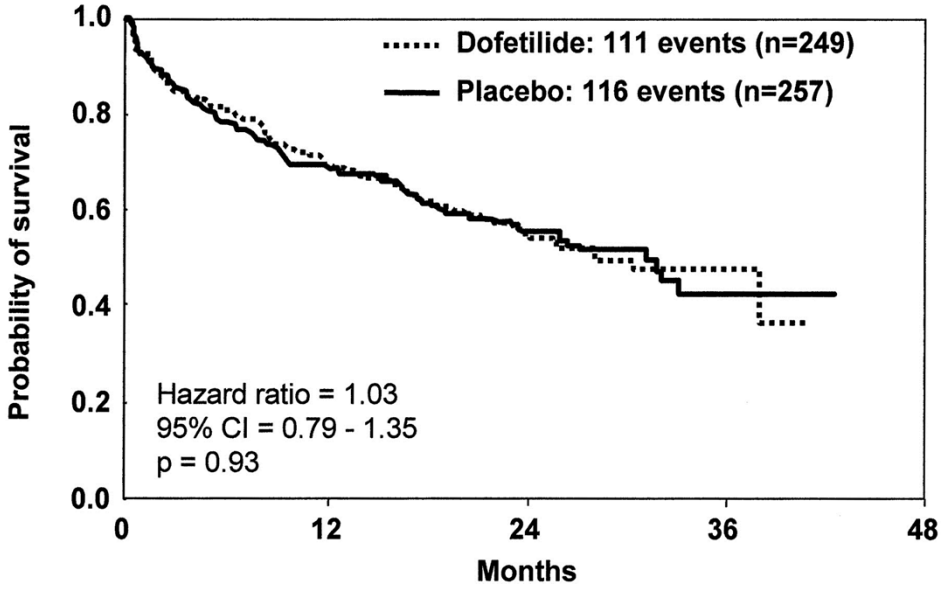
682 in rhythm-control and 694 in rate-control and EF<35% , 37 month F/U
Age 66±11 vs 67 ±11 yr

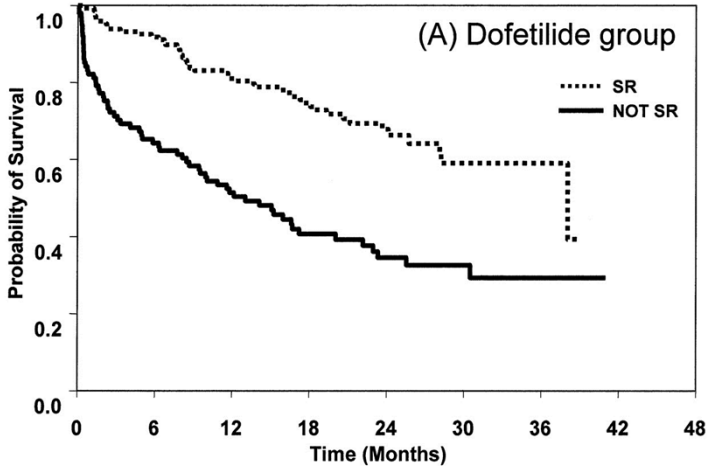


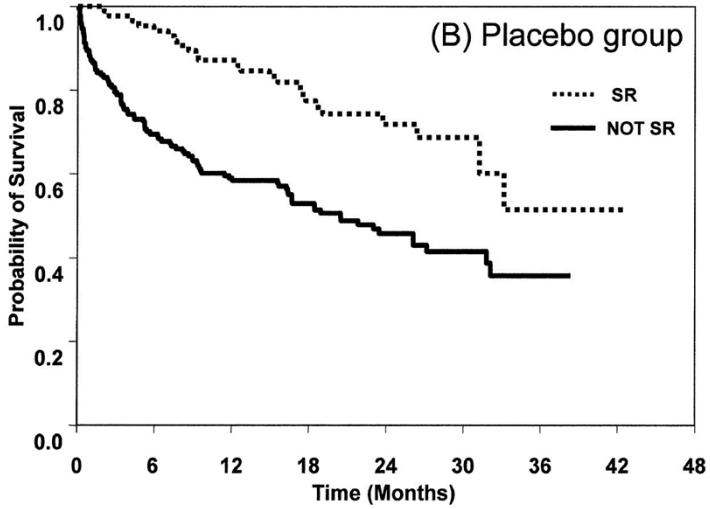
Roy D et al. N Engl J Med 2008;358:2667-2677.

Danish Investigations of Arrhythmia and Mortality ON Dofetilide (DIAMOND) Substudy

HF pt=506



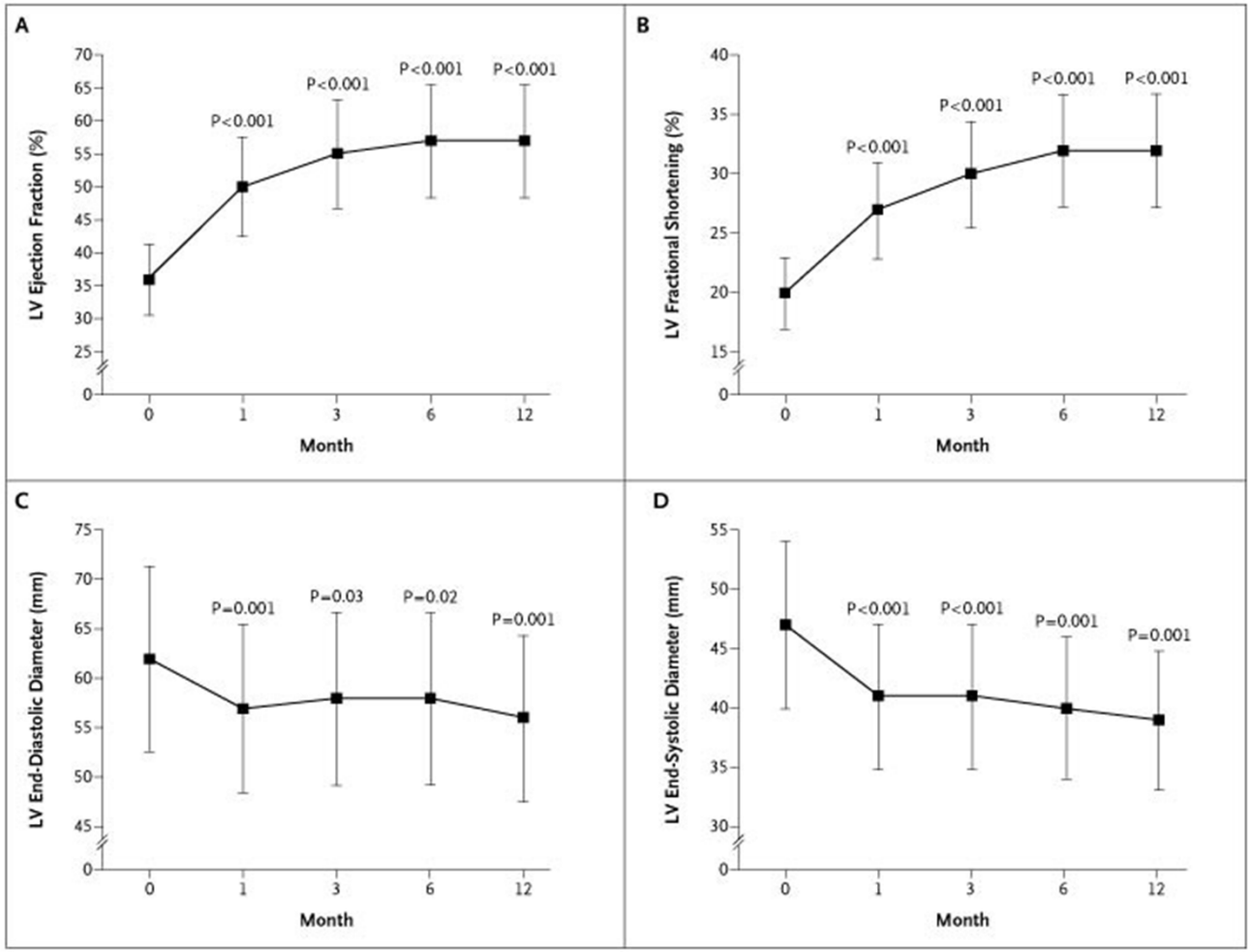




Pedersen, O. D. et al. Circulation 2001;104:292-296

Improvement in LV Function and Dimensions after Catheter Ablation in Patients with CHF

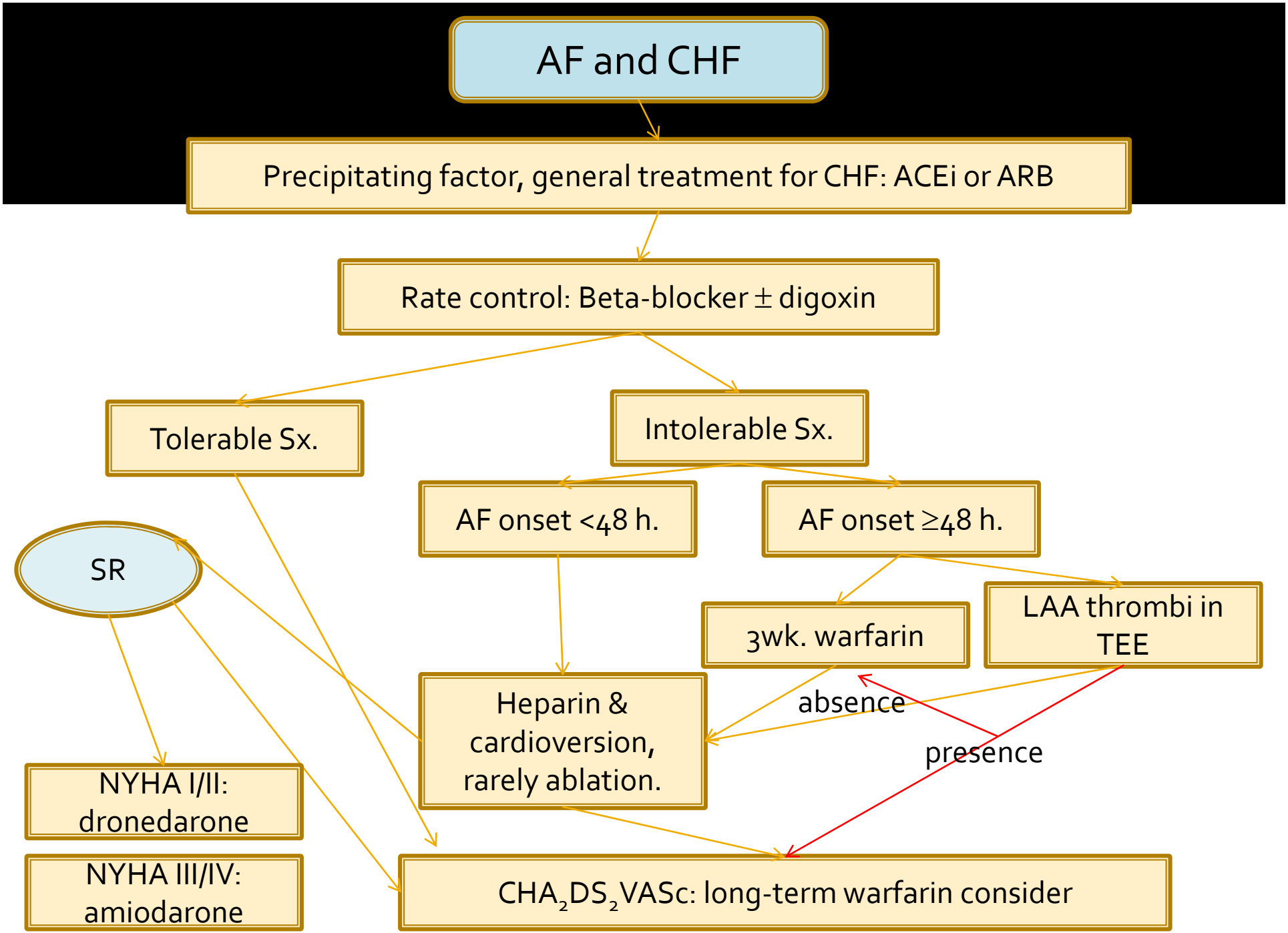
Catheter Ablation is promising strategy in pt with CHF



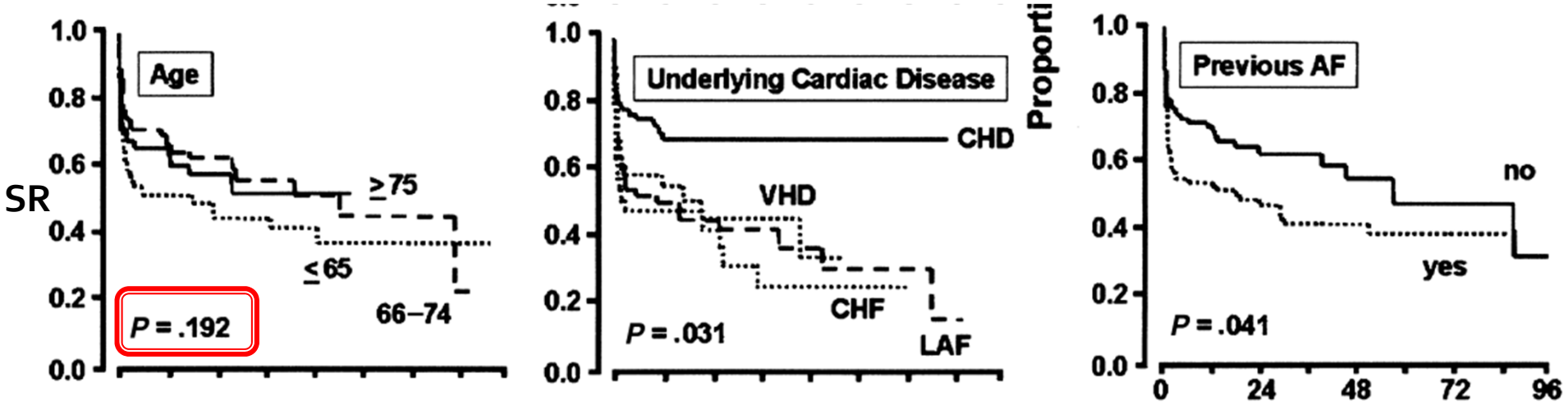
Hsu L et al. N Engl J Med 2004;351:2373-2383.

Occurrence of AF and HF in aging

1. Lone AF
   - CHF
2. CHF
   - AF
3. CHF
   - Permanent AF
4. ~~4~~
   - AF
   - CHF


AF and CHF
Precipitating factor, general treatment for CHF: ACEi or ARB
Rate control: Beta-blocker ± digoxin
Tolerable Sx.
Intolerable Sx.
AF onset <48 h.
AF onset ≥48 h.
SR
3wk. warfarin
LAA thrombi in TEE
Heparin & cardioversion, rarely ablation.
absence
presence
NYHA I/II: dronedarone
NYHA III/IV: amiodarone
CHA2DS2VASc: long-term warfarin consider

Does Advanced Age Affect the Immediate and Long-Term Results of Direct-Current External Cardioversion of AF?



Fumagalli S, J Am Geriat Soc 2002:50:1192-1197

Conclusion

- AF and CHF is common CV disease in the elderly
- Inter-relationship between AF and CHF is complex
- Anticoagulation is more important for the protection of stroke from the elderly with AF.
- AF may be a marker of frailty in the elderly
- Age-oriented guideline is necessary to effectively manage AF in the elderly