Advances in Cardiac Arrhythmias and Great innovations in Cardiology
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Arrhythmias and cardiomyopathy : Which condition comes first?

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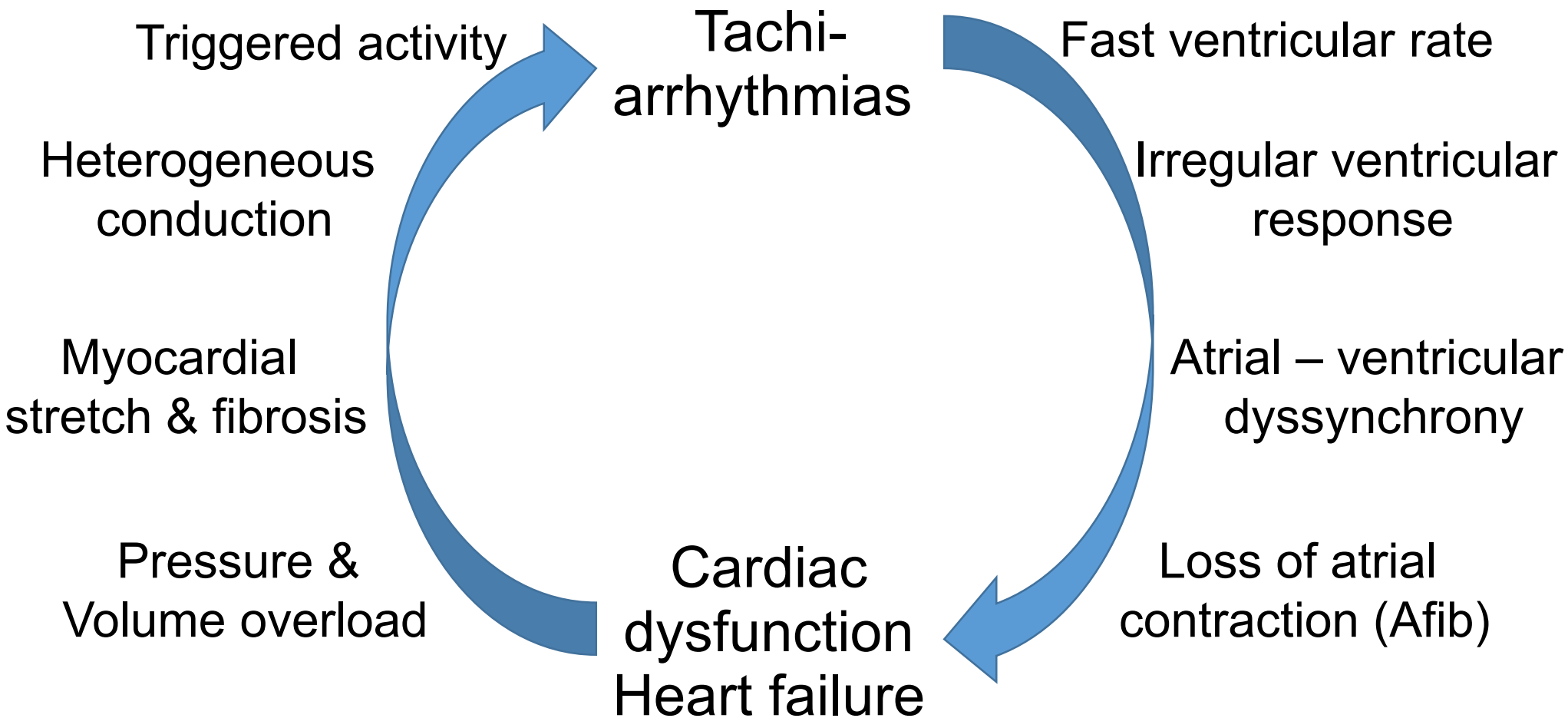
Tachyarrhythmias and Heart Failure: Which comes first?



Arrhythmia Induced Cardiomyopathy (AIC) or Tachycardiomyopathy

- An impairment of LV function caused by atrial or ventricular tachyarrhythmias, partially or completely reversible after normalization of the heart rate.

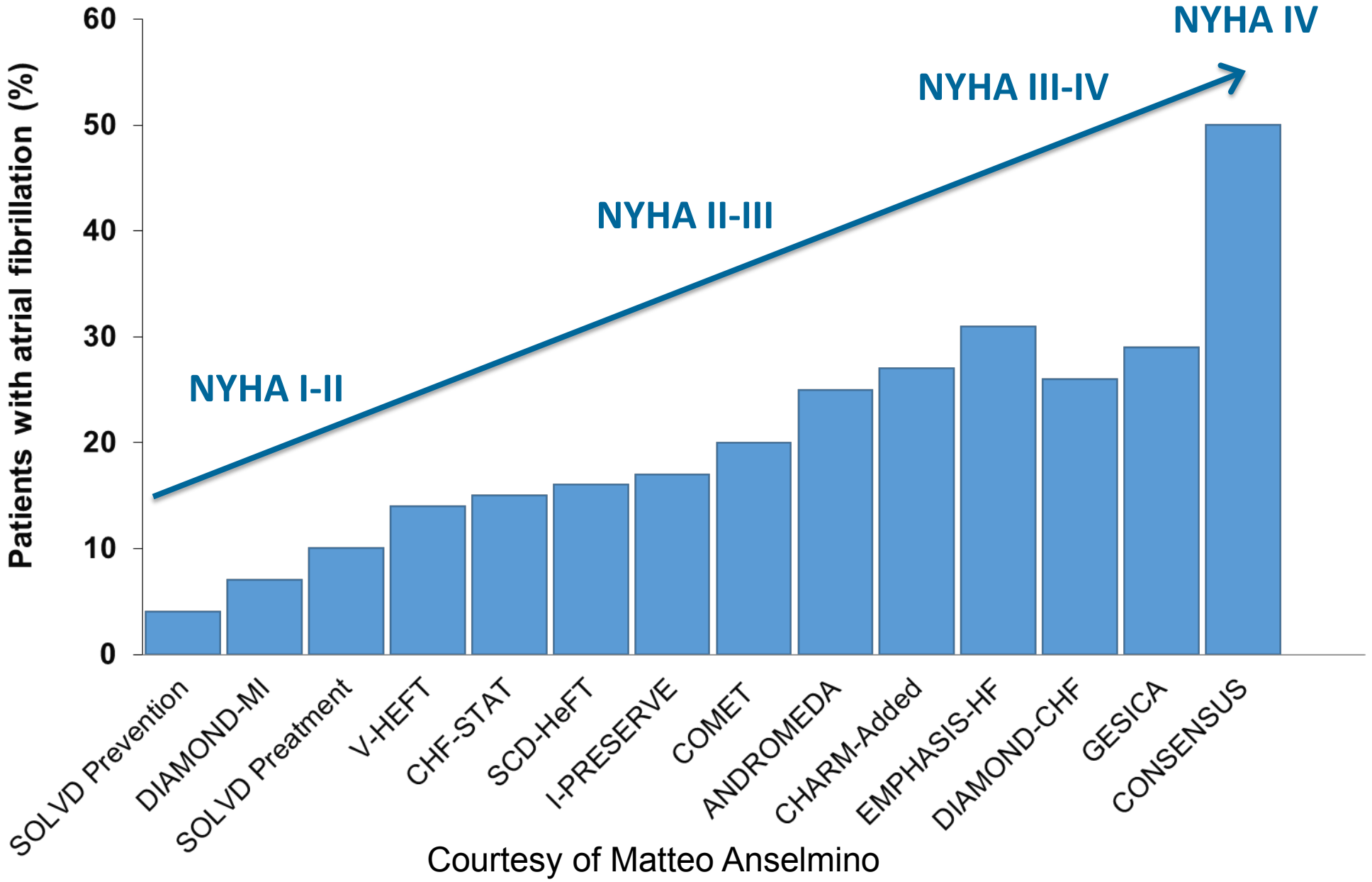
- **Pure or arrhythmia induced**
  - The only cause of the myocardial dysfunction
- **Impure or arrhythmia mediated**
  - The arrhythmia exacerbates ventricular dysfunction and HF in a patient with concomitant heart disease

Fenelon G, Wijns W, Andries E, Brugada P. PACE. 1996;19(1):95-106.
Gopinathannair R et al. J Am Coll Cardiol 2015;66(15):1714-28.

Arrhythmias causing AIC

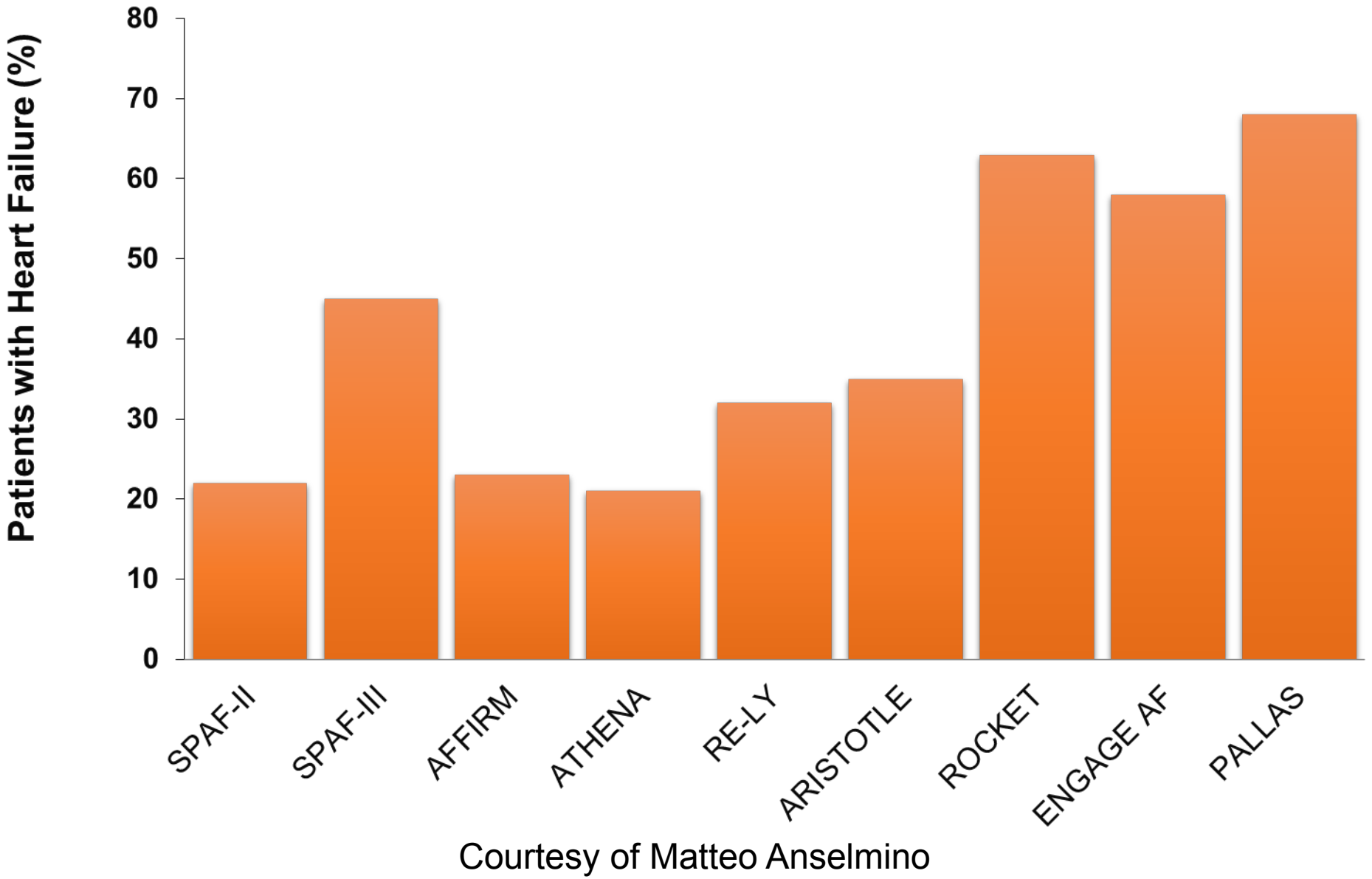
- Supraventricular
  - Atrial fibrillation/ flutter/ tachycardia
  - Permanent AV reentrant tachycardia
  - Inappropriate sinus tachycardia (rare)
- Ventricular
  - Right ventricular outflow tract ventricular tachycardia
  - Fascicular tachycardia
  - Bundle branch reentry ventricular tachycardia
- Ectopy
  - Frequent PVCs
- Pacing
  - Persistent rapid atrial or ventricular pacing

Prevalence of AF in HF trials



Courtesy of Matteo Anselmino

Prevalence of HF in AF trials



Courtesy of Matteo Anselmino

Atrial Fibrillation Begets Heart Failure and Vice Versa

Temporal Associations and Differences in Preserved Versus Reduced Ejection Fraction

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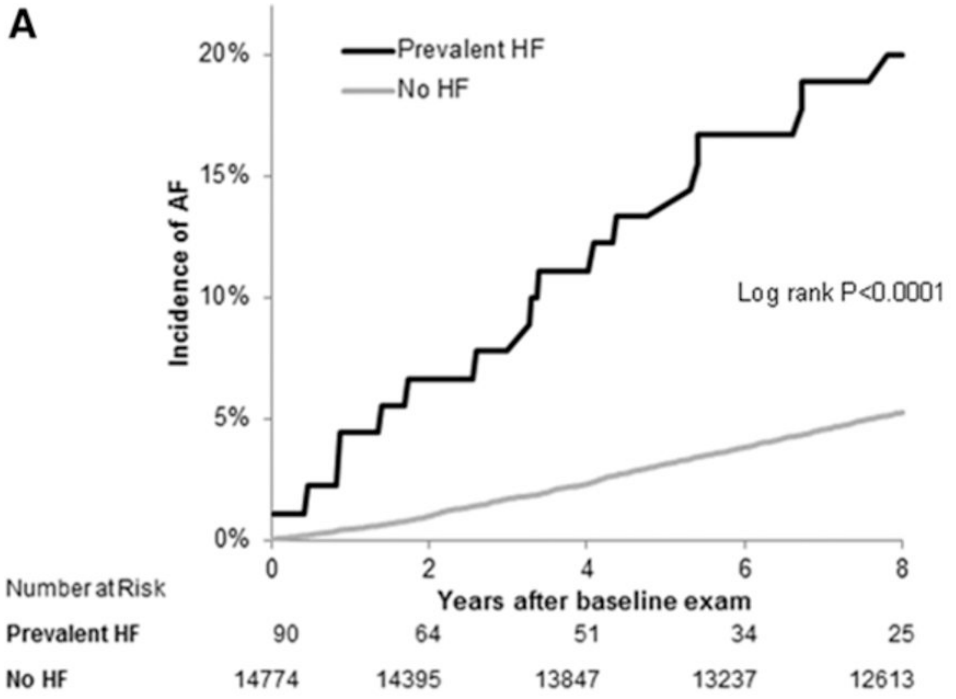
Background—Atrial fibrillation (AF) and heart failure (HF) frequently coexist and together confer an adverse prognosis. The association of AF with HF subtypes has not been well described. We sought to examine differences in the temporal association of AF and HF with preserved versus reduced ejection fraction.

Methods and Results—We studied Framingham Heart Study participants with new-onset AF or HF between 1980 and 2012. Among 1737 individuals with new AF (mean age, 75±12 years; 48% women), more than one third (37%) had HF. Conversely, among 1166 individuals with new HF (mean age, 79±11 years; 53% women), more than half (57%) had AF. Prevalent AF was more strongly associated with incident HF with preserved ejection fraction (multivariable-adjusted hazard ratio [HR], 2.34; 95% confidence interval [CI], 1.48–3.70; no AF as referent) versus HF with reduced ejection fraction (HR, 1.32; 95% CI, 0.83–2.10), with a trend toward difference between HF subtypes (*P* for difference=0.06). Prevalent HF was associated with incident AF (HR, 2.18; 95% CI, 1.26–3.76; no HF as referent). The presence of both AF and HF portended greater mortality risk compared with neither condition, particularly among individuals with new HF with reduced ejection fraction and prevalent AF (HR, 2.72; 95% CI, 2.12–3.48) compared with new HF with preserved ejection fraction and prevalent AF (HR, 1.83; 95% CI, 1.41–2.37; *P* for difference=0.02).

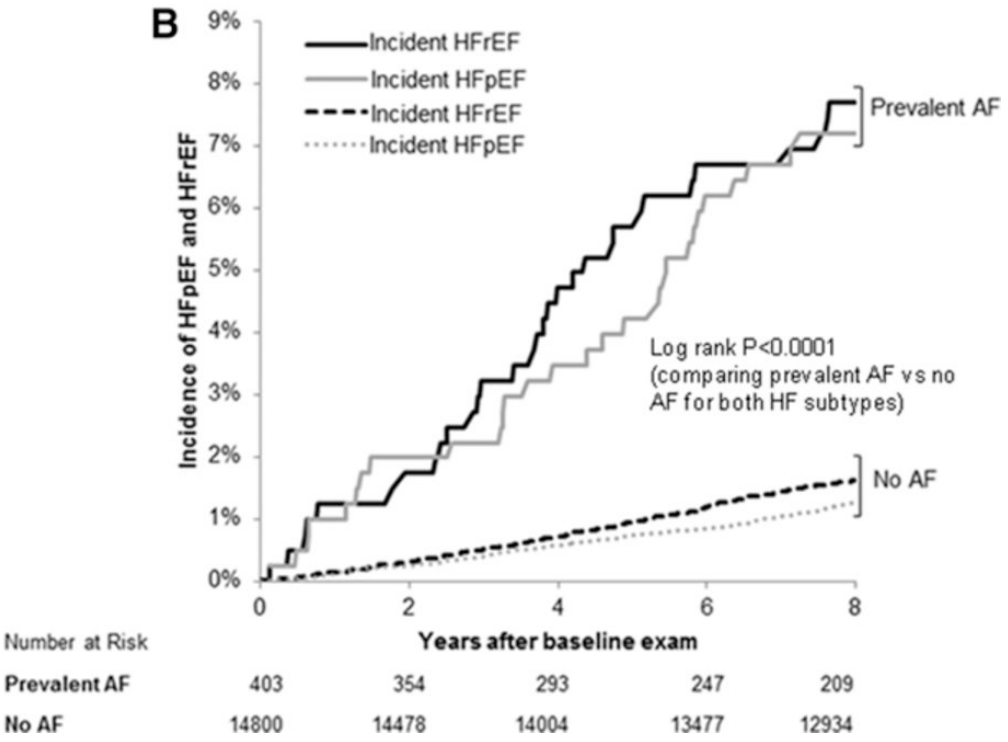
Conclusions—AF occurs in more than half of individuals with HF, and HF occurs in more than one third of individuals with AF. AF precedes and follows HF with both preserved and reduced ejection fraction, with some differences in temporal association and prognosis. Future studies focused on underlying mechanisms of these dual conditions are warranted.
(***Circulation***. **2016;133:484-492. DOI: 10.1161/CIRCULATIONAHA.115.018614.**)

Cumulative incidence of atrial fibrillation (AF) and heart failure (HF) among those with and without the other condition.

Incidence of AF (n=795)

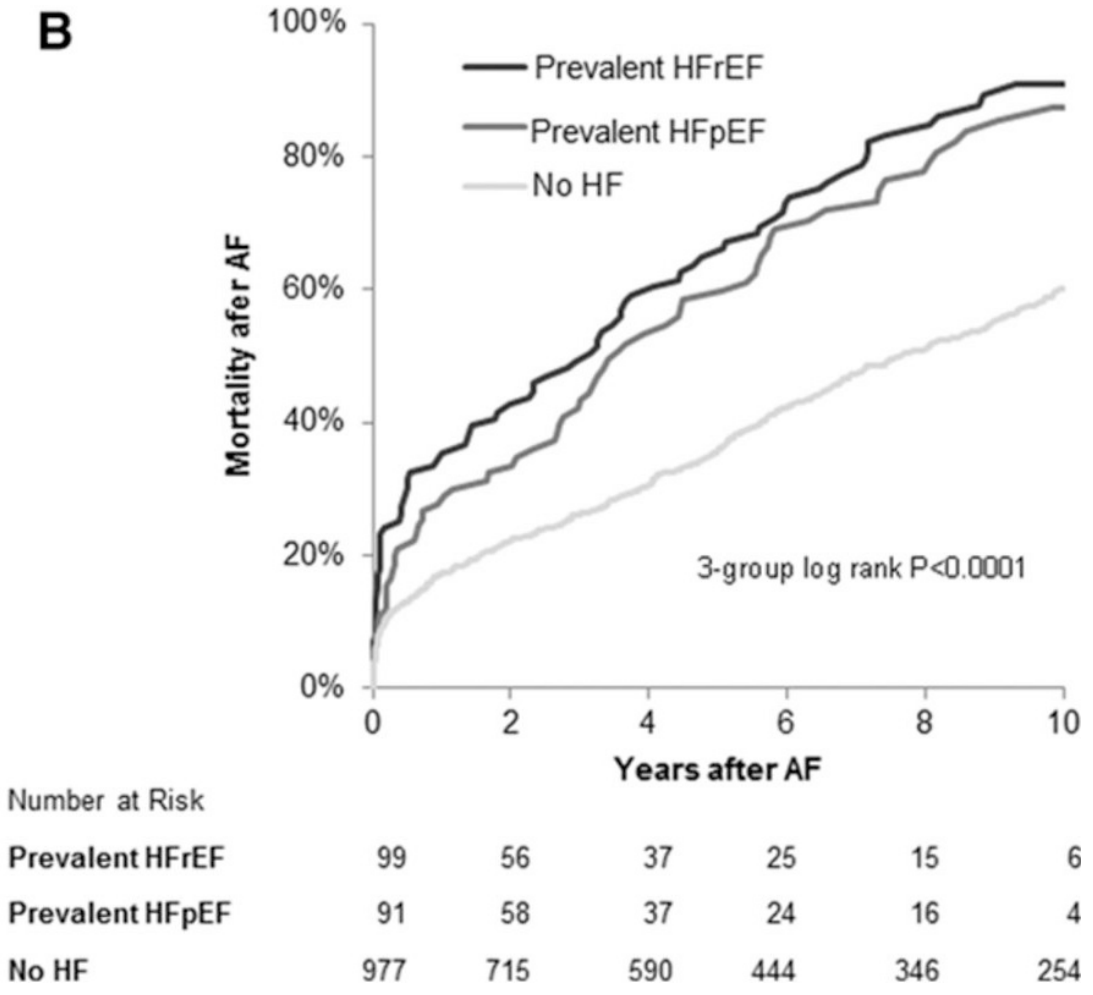


Incidence of HF (n=487)



Rajalakshmi Santhanakrishnan et al. Circulation. 2016;133:484-492

All-cause mortality after new onset atrial fibrillation (AF)



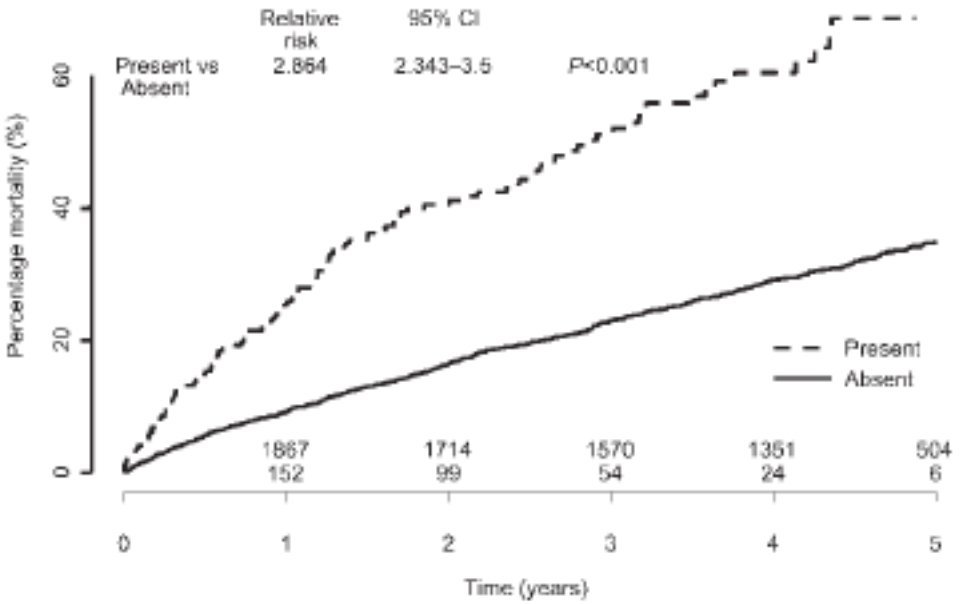
Rajalakshmi Santhanakrishnan et al. Circulation. 2016;133:484-492

European Heart Journal (2005) 26, 1303–1308
doi:10.1093/eurheartj/ehi166

Clinical research

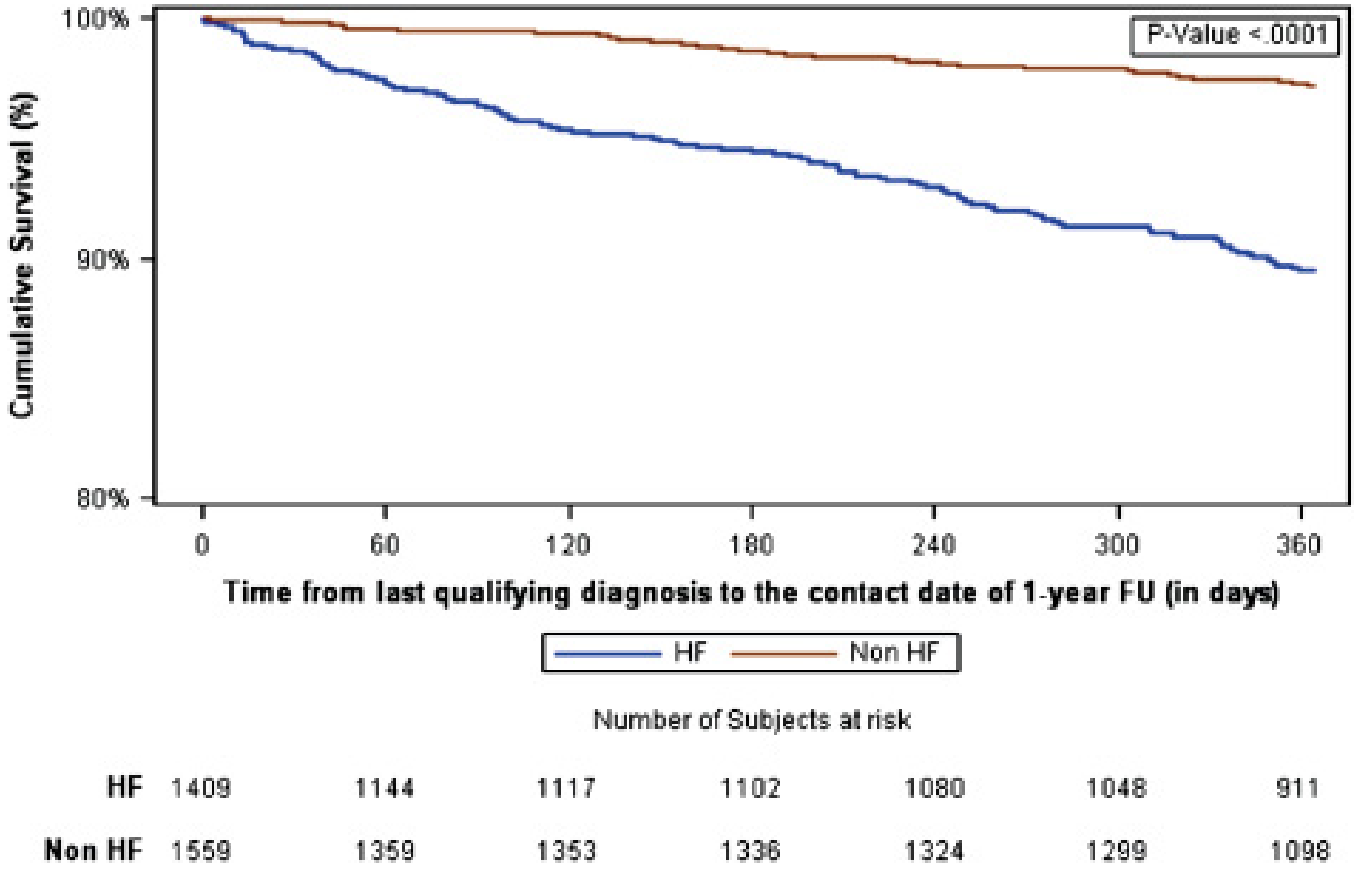
Prognostic relevance of atrial fibrillation in patients with chronic heart failure on long-term treatment with beta-blockers: results from COMET

Karl Swedberg[1*], Lars G. Olsson[1], Andrew Charlesworth[2], John Cleland[3], Peter Hanrath[4], Michel Komajda[5], Marco Metra[6], Christian Torp-Pedersen[7], and Philip Poole-Wilson[8]



Conclusion In CHF, atrial fibrillation significantly increases the risk for death and heart failure hospitalization, but is not an independent risk factor for mortality after adjusting for other predictors of prognosis. Treatment with carvedilol compared with metoprolol offers additional benefits among patients with atrial fibrillation. Onset of new atrial fibrillation in patients on long-term beta-blocker therapy is associated with significant increased subsequent risk of mortality and morbidity.

Heart failure in patients with atrial fibrillation in Europe: a report from the EURObservational Research Programme Pilot survey on AF



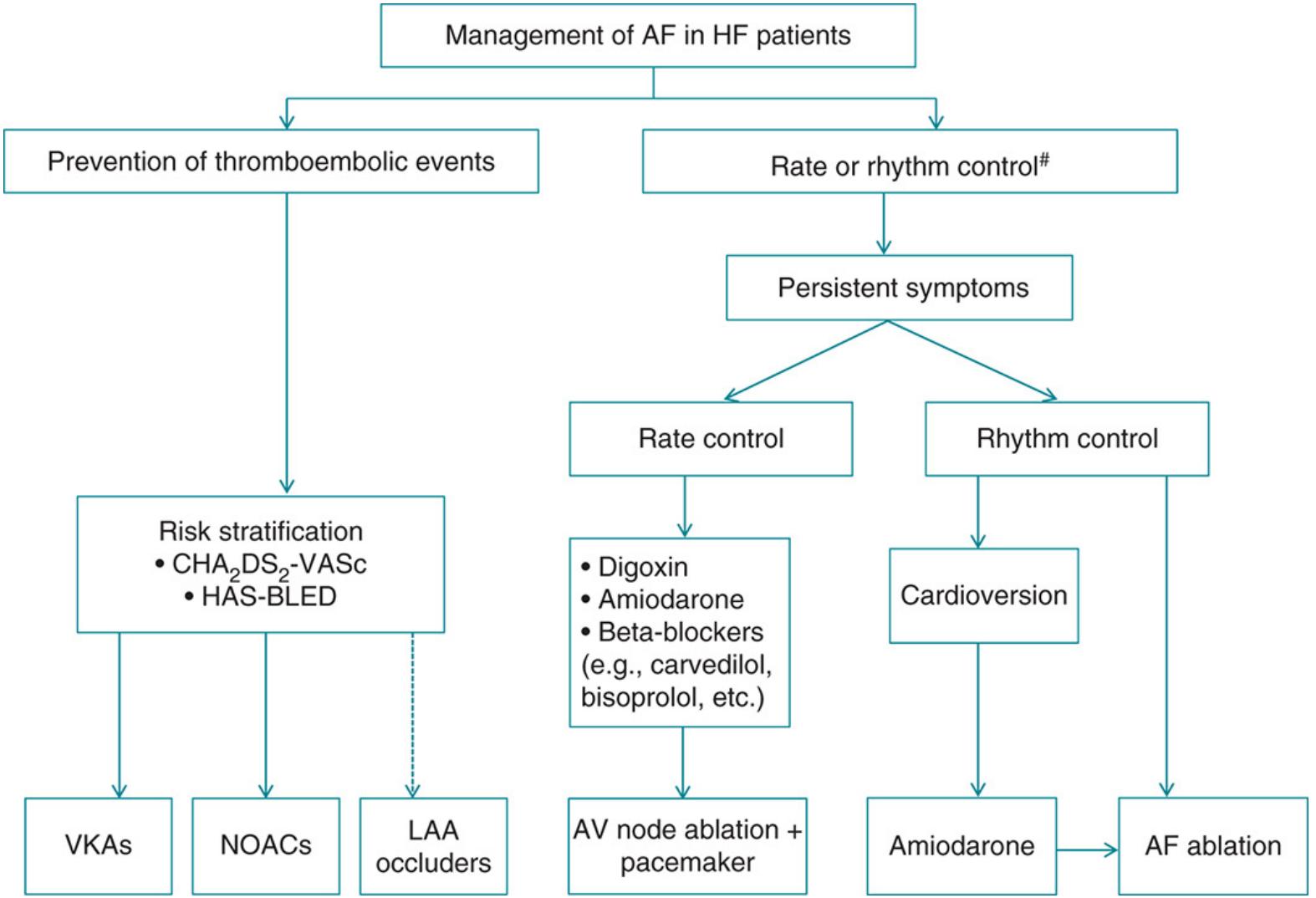
Lip et al. European Journal of Heart Failure 215; 17: 570-582

Criteria for a possible diagnosis of AIC

- New onset of LV dysfunction
- Chronic or recurrent tachycardia with HR > 100 beats per minute
- No signs of acute coronary syndrome or other causes of non-ischemic cardiomyopathy
- Absence of LV hypertrophy as a possible cause of HF
- Normal LV dimensions
- Recovery of LV function after control of tachycardia within 1-6 months
- Rapid decline in LVEF following recurrence of tachycardia in a patient with a previous recovery of LV function after tachycardia control

Modified from Gupta et al. Int J Cardiol. 2014;172:40-6.

Management of atrial fibrillation in heart failure patients



Lip et al. Eur J Heart Fail 2015; 17: 848-874

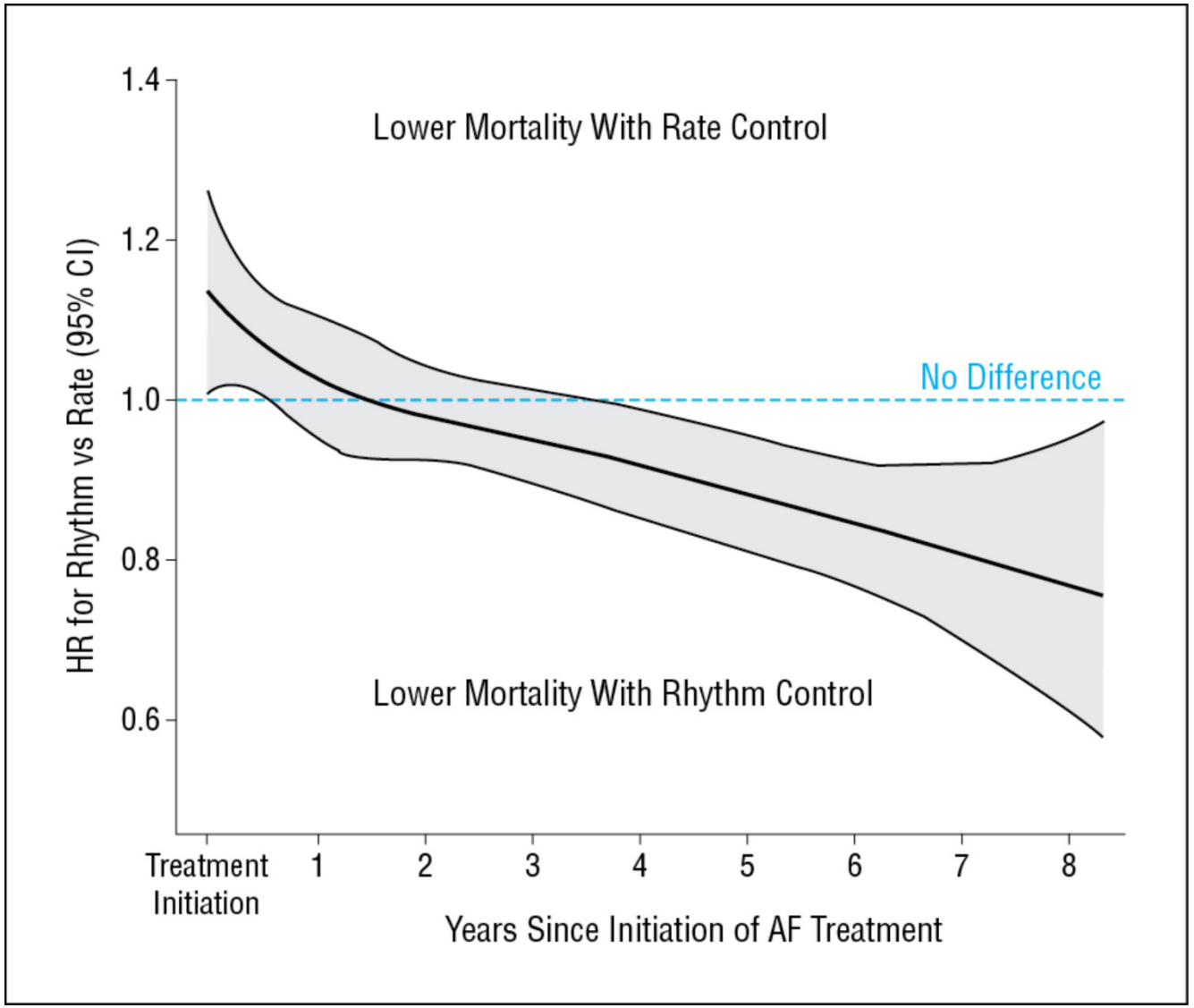
Rate control vs. Rhythm control trials

Trial	Inclusion criteria	Primary outcome Parameter	Patients reaching primary outcome (n)		
			Rate ctrl	Rhytm ctrl	P
PIAF (2000) 252 Patients	Persistent AF (7-360 days)	Symptomatic improvement	76/125 (60.8%)	70/127 (55.1%)	0.32
AFFIRM (2002) 4060 Patients	Paroxysmal AF or persistent AF, age ≥65 years, or risk of stroke or death	All-cause mortality	310/2027 (25.9%)	356/2033 (26.7%)	0.08
RACE (2002) 522 Patients	Persistent AF or flutter for <1 year and 1-2 cardioversions over 2 years and oral anticoagulation	Composite: cardiovascular death, CHF, severe bleeding, pacemaker implantatation, thrombo-embolic events, severe adverse effects of antiarrhyt. drugs	44/256 (17.2%)	60/266 (22.6%)	0.11
STAF (2003) 200 Patients	Persistent AF (>4 weeks and <2 years), LA size >45 mm, CHF NYHA II-IV, LVEF <45%	Composite: overall mortality, cerebrovascular complications, CPR, embolic events	10/100 (10.0%)	9/100 (9.0%)	0.99
HOT CAFÈ (2004) 205 Patients	First clinically overt persistent AF (≥7 days and <2 years), age 50-75 years	Composite: death, thrombo-embolic events; intracranial/major haemorrhage	1/101 (1.0%)	4/104 (3.9%)	>0.71
AF-CHF (2008) 1376 Patients	LVEF ≤35%, symptoms of CHF, history of AF (≥6 h or DCC <last 6 months)	Cardiovascular death	175/1376 (25%)	182/1376 (27%)	0.59
J-RHYTHM (2009) 823 Patients	Paroxysmal AF	Composite of total mortality, symptomatic cerebral infarction, systemic embolism, major bleeding, hospitalization for heart failure, or physical/psychological disability	89/405 (22.0%)	64/418 (15.3%)	0.012

Rhythm control versus Rate control in patients with AF and HF

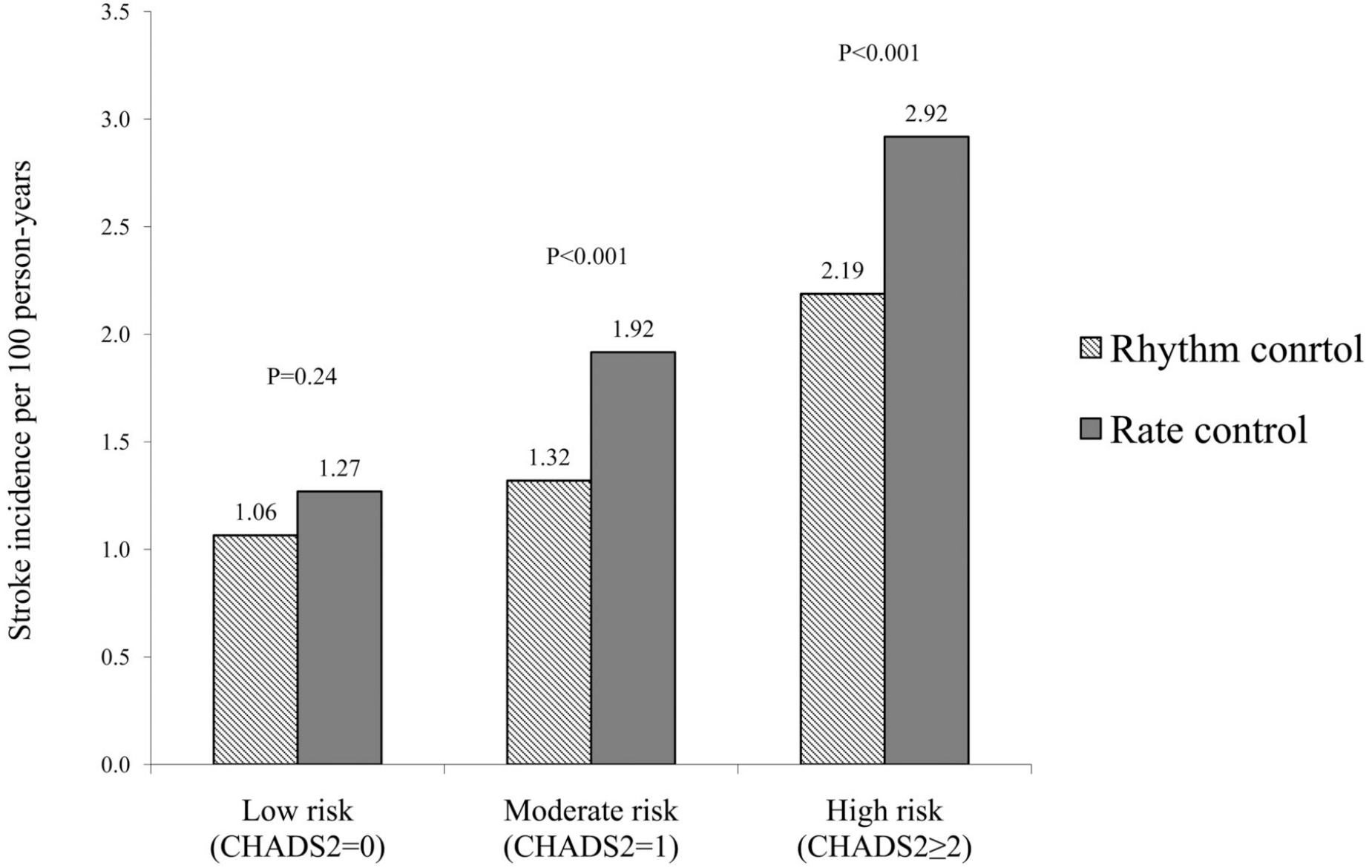
- No evidence from RCTs favoring either strategy
- Large observational studies have suggested a benefit of the rhythm control strategy on long-term mortality and stroke rates.
- In RCTs up to 40% of the patients were in sinus rhythm in the rate control group.
- The untoward effects of antiarrhytmic drugs may have worsened outcomes in the rhythm control group

Effects on mortality of rhythm vs rate control strategy in patients with atrial fibrillation (26.130 subjects in a population-based administrative database from Quebec)



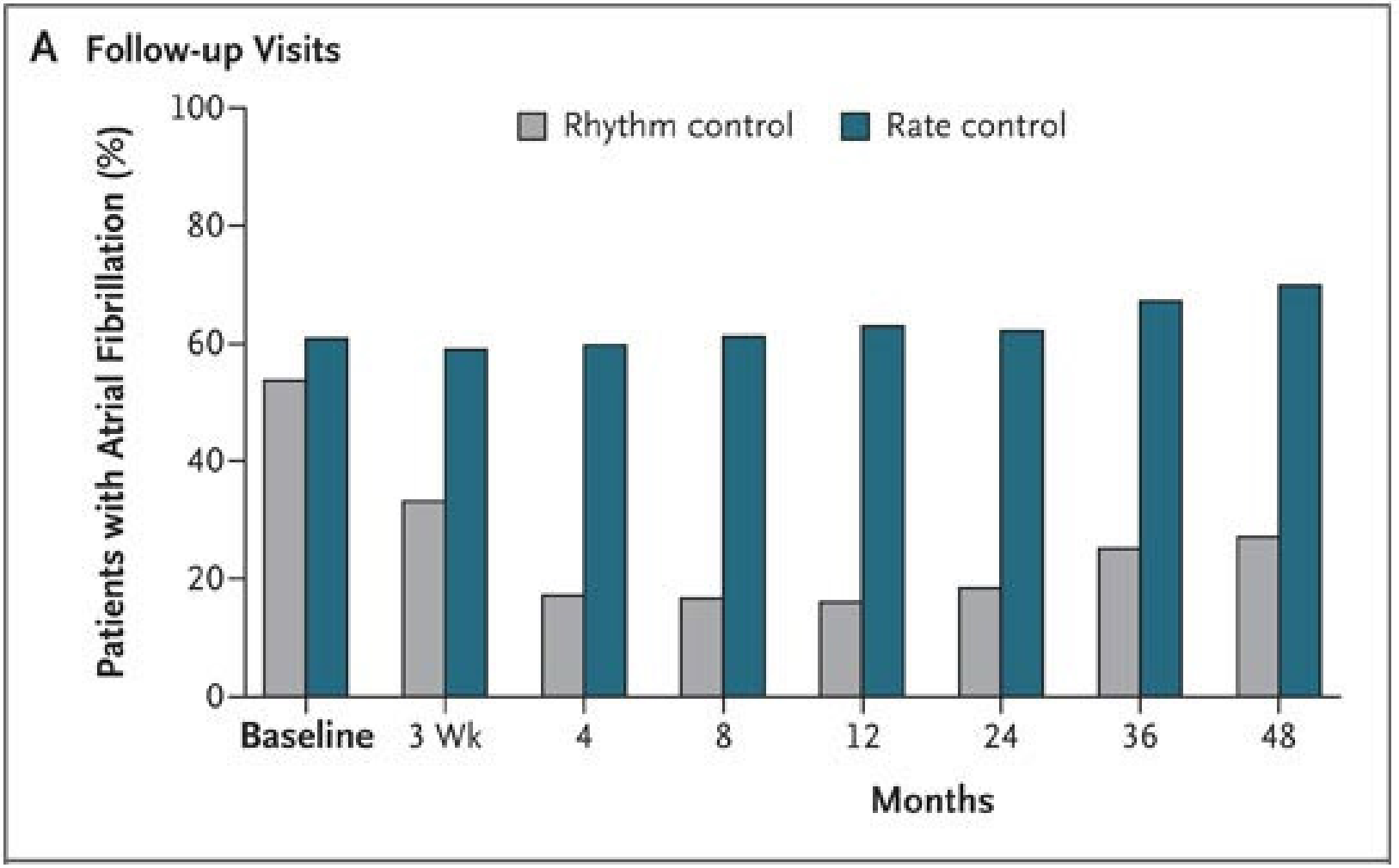
Ionescu-Ittu et al. Arch Intern Med. 2012;172(13):997-1004.

Crude incidence rates of stroke/TIA by CHADS2 score. Population-based observational study in Quebec



Meytal Avgil Tsadok et al. Circulation. 2012;126:2680-2687

AF-CHF Trial. Prevalence of Atrial Fibrillation at Each Follow-up Visit



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

AF-CHF Trial. Medical Therapy at 12 Months

Table 2. Medical Therapy at 12 Months.*

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

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

Catheter Ablation of Atrial Fibrillation in Patients With Left Ventricular Systolic Dysfunction

A Systematic Review and Meta-Analysis

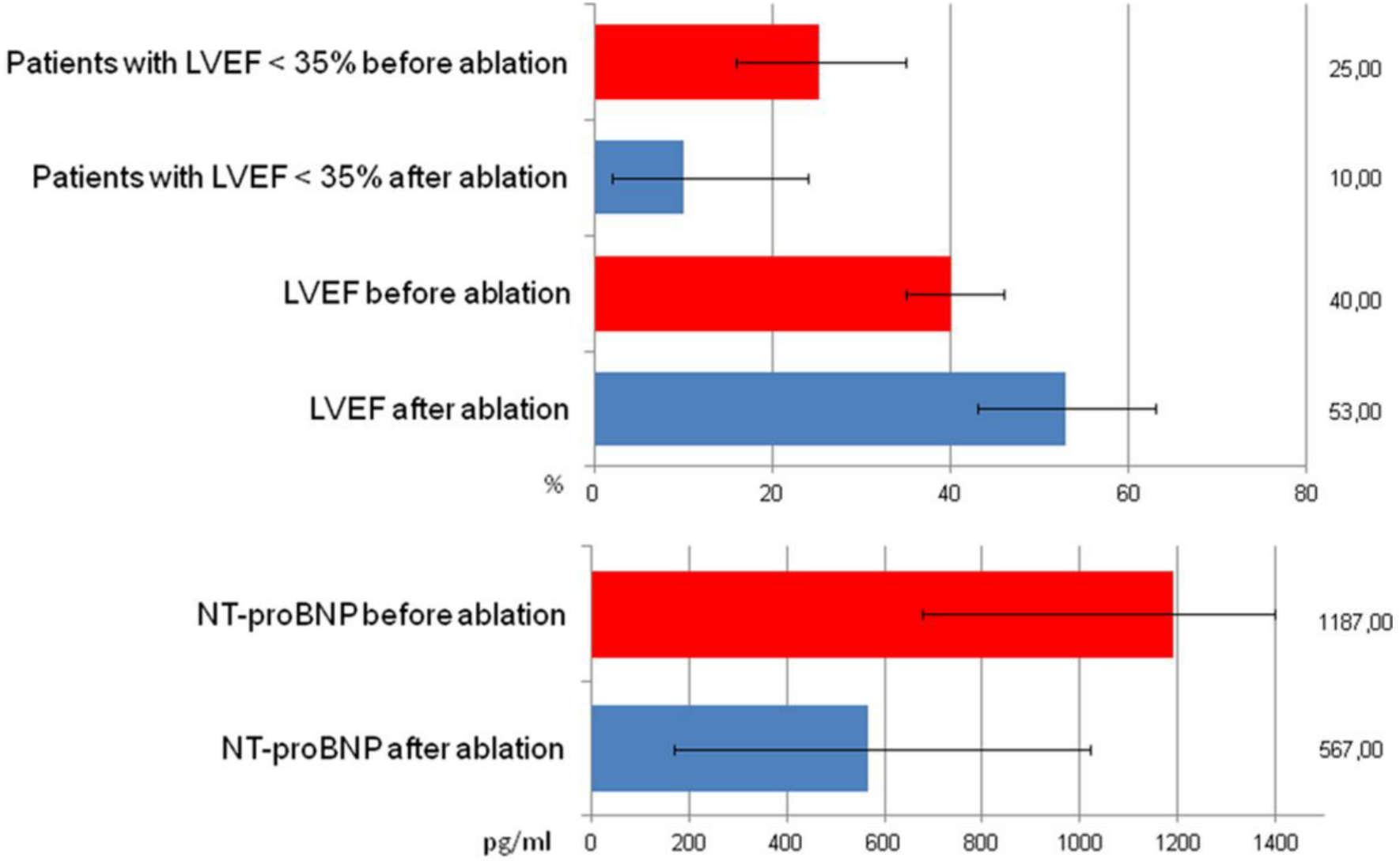
Matteo Anselmino, MD, PhD; Mario Matta, MD; Fabrizio D'Ascenzo, MD; T. Jared Bunch, MD; Richard J. Schilling, MD; Ross J. Hunter, MD, PhD; Carlo Pappone, MD, PhD; Thomas Neumann, MD; Georg Noelker, MD; Martin Fiala, MD, PhD; Emanuele Bertaglia, MD; Antonio Frontera, MD; Edward Duncan, MD; Chrishan Nalliah, BSc, MBBS; Pierre Jais, MD; Rukshen Weerasooriya, MD; Jon M. Kalman, MD, PhD; Fiorenzo Gaita, MD

Background—Catheter ablation of atrial fibrillation (AFCA) is an established therapeutic option for rhythm control in symptomatic patients. Its efficacy and safety among patients with left ventricular systolic dysfunction is based on small populations, and data concerning long-term outcome are limited. We performed this meta-analysis to assess safety and long-term outcome of AFCA in patients with left ventricular systolic dysfunction, to evaluate predictors of recurrence and impact on left ventricular function.

Methods and Results—A systematic review was conducted in MEDLINE/PubMed and Cochrane Library. Randomized controlled trials, clinical trials, and observational studies including patients with left ventricular systolic dysfunction undergoing AFCA were included. Twenty-six studies were selected, including 1838 patients. Mean follow-up was 23 (95% confidence interval, 18–40) months. Overall complication rate was 4.2% (3.6%–4.8%). Efficacy in maintaining sinus rhythm at follow-up end was 60% (54%–67%). Meta-regression analysis revealed that time since first atrial fibrillation (P=0.030) and heart failure (P=0.045) diagnosis related to higher, whereas absence of known structural heart disease (P=0.003) to lower incidence of atrial fibrillation recurrences. Left ventricular ejection fraction improved significantly during follow-up by 13% (P<0.001), with a significant reduction of patients presenting an ejection fraction <35% (P<0.001). N-terminal pro-brain natriuretic peptide blood levels decreased by 620 pg/mL (P<0.001).

Conclusions—AFCA efficacy in patients with impaired left ventricular systolic function improves when performed early in the natural history of atrial fibrillation and heart failure. AFCA provides long-term benefits on left ventricular function, significantly reducing the number of patients with severely impaired systolic function. (***Circ Arrhythm Electrophysiol.* 2014;7:1011-1018.**)

Improvement in cardiac function after atrial fibrillation catheter ablation



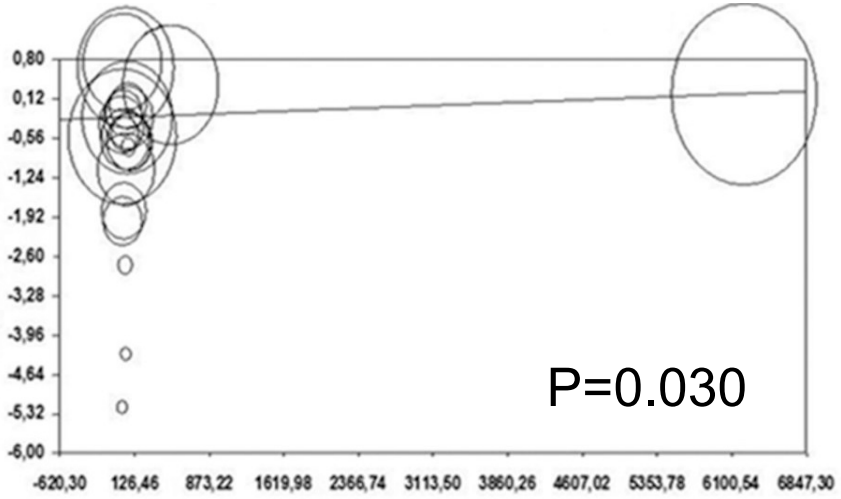
Matteo Anselmino et al. Circ Arrhythm Electrophysiol. 2014;7:1011-1018

Catheter Ablation of Atrial Fibrillation in Patients With Left Ventricular Systolic Dysfunction

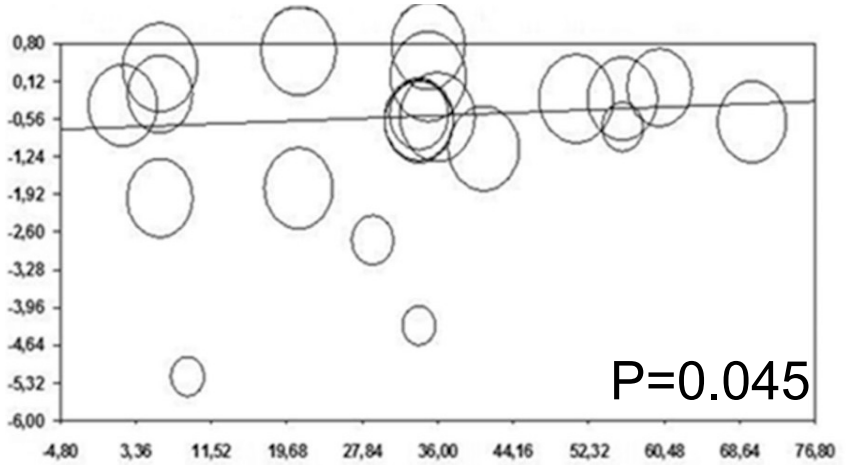
A Systematic Review and Meta-Analysis

Predictors of AF Recurrence

Time since first AF diagnosis

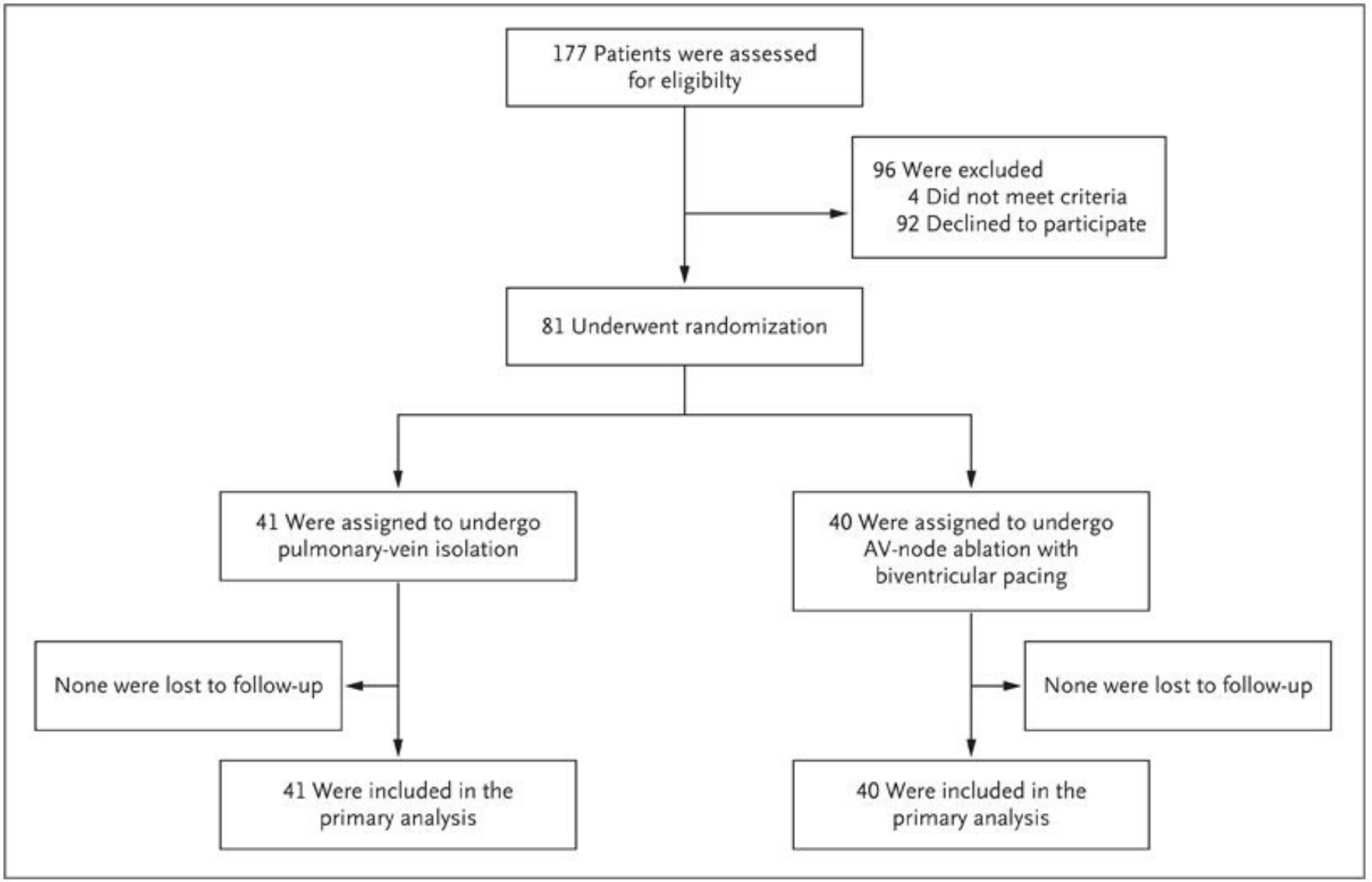


Time since first HF diagnosis



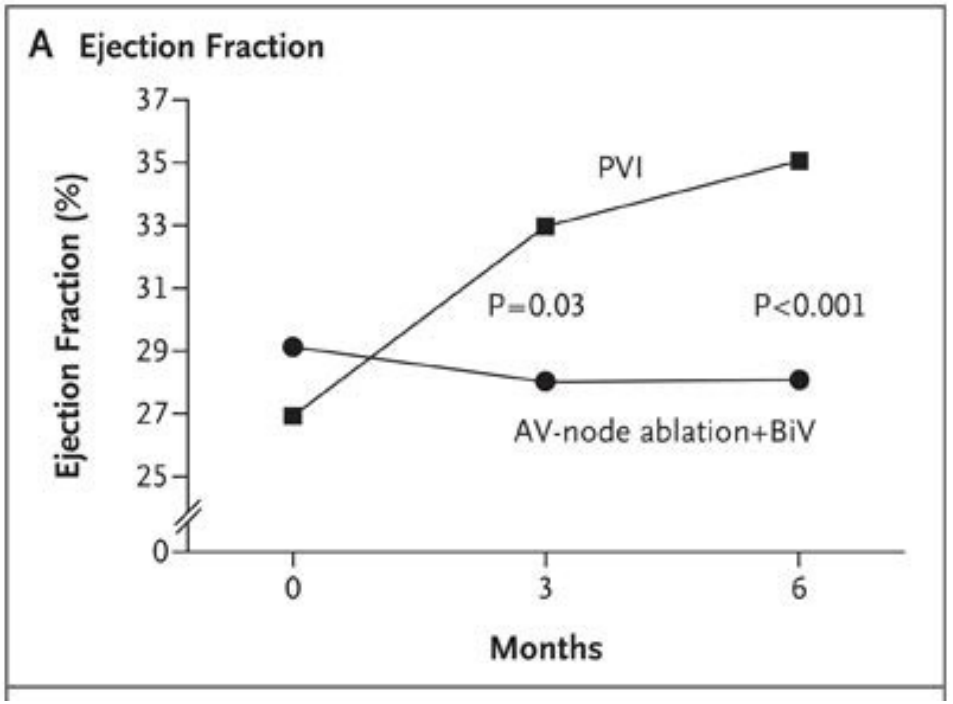
Anselmino M et al. Circ Arrhythm Electrophysiol 2014; 7: 1011-1018

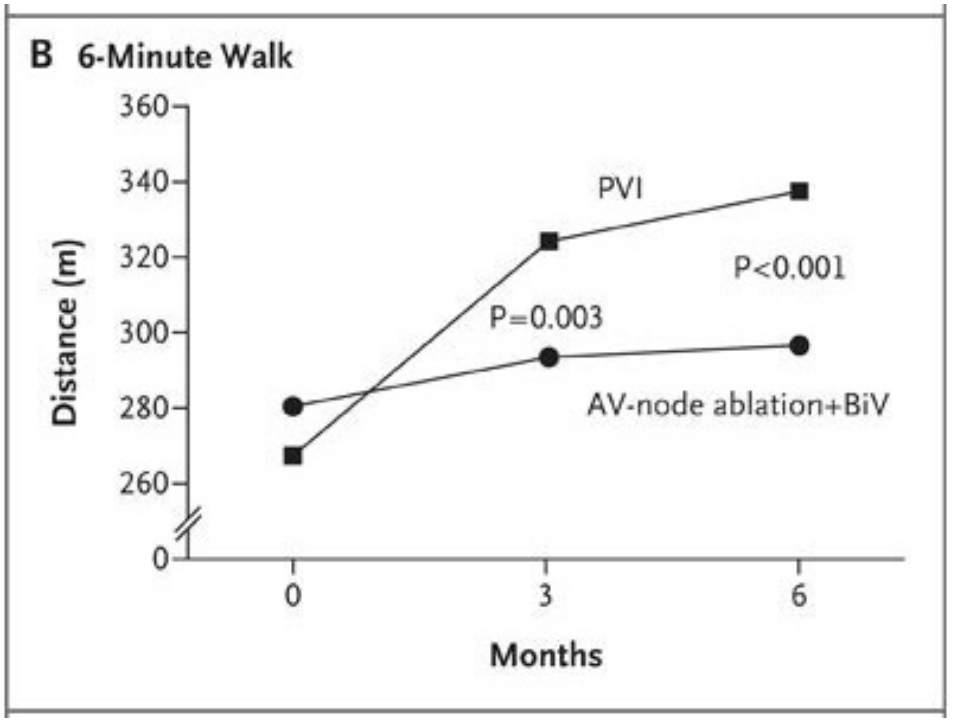
PABA-CHF. Enrollment and Follow-up of Study Patients



Khan MN et al. N Engl J Med 2008;359:1778-1785.

Ejection Fraction and 6-Minute Walk Distance at 6 Months.





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European Journal of Heart Failure (2013) **15**, 1311–1318
doi:10.1093/eurjhf/hft093

Lenient vs. strict rate control in patients with atrial fibrillation and heart failure: a post-hoc analysis of the RACE II study

Bart A. Mulder[1], Dirk J. Van Veldhuisen[1], Harry J.G.M. Crijns[2], Jan G.P. Tijssen[3], Hans L. Hillege[4], Marco Alings[5], Michiel Rienstra[1], Hessel F. Groenveld[1], Maarten P. Van den Berg[1], and Isabelle C. Van Gelder[1,6]* for the RACE II investigators†

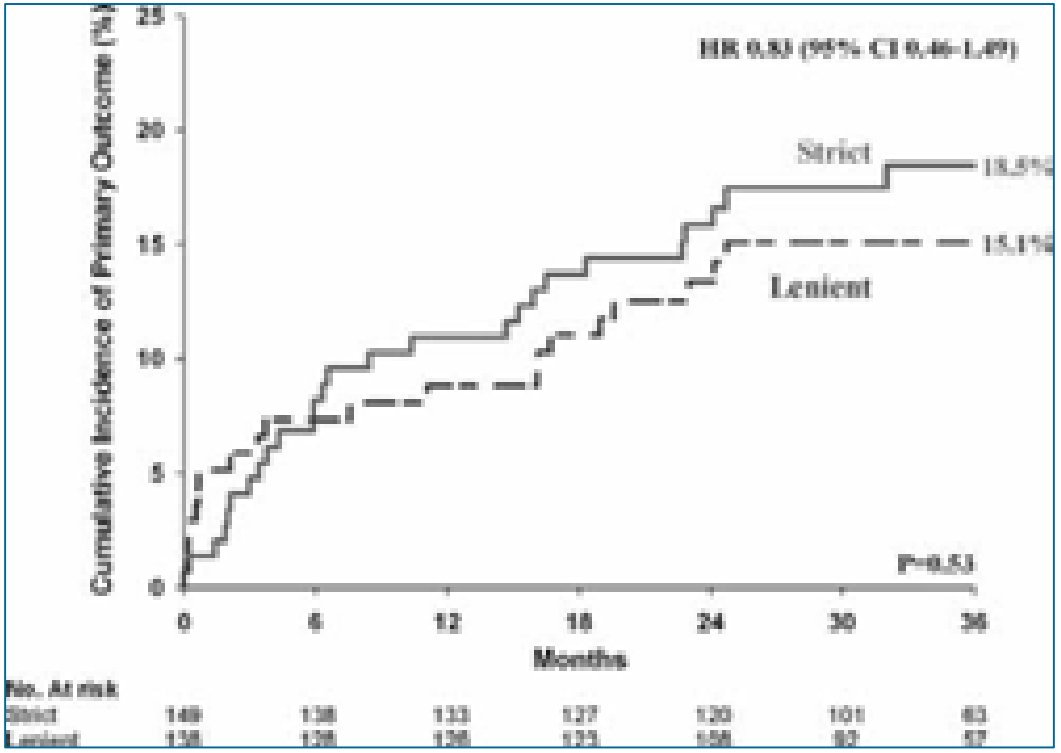

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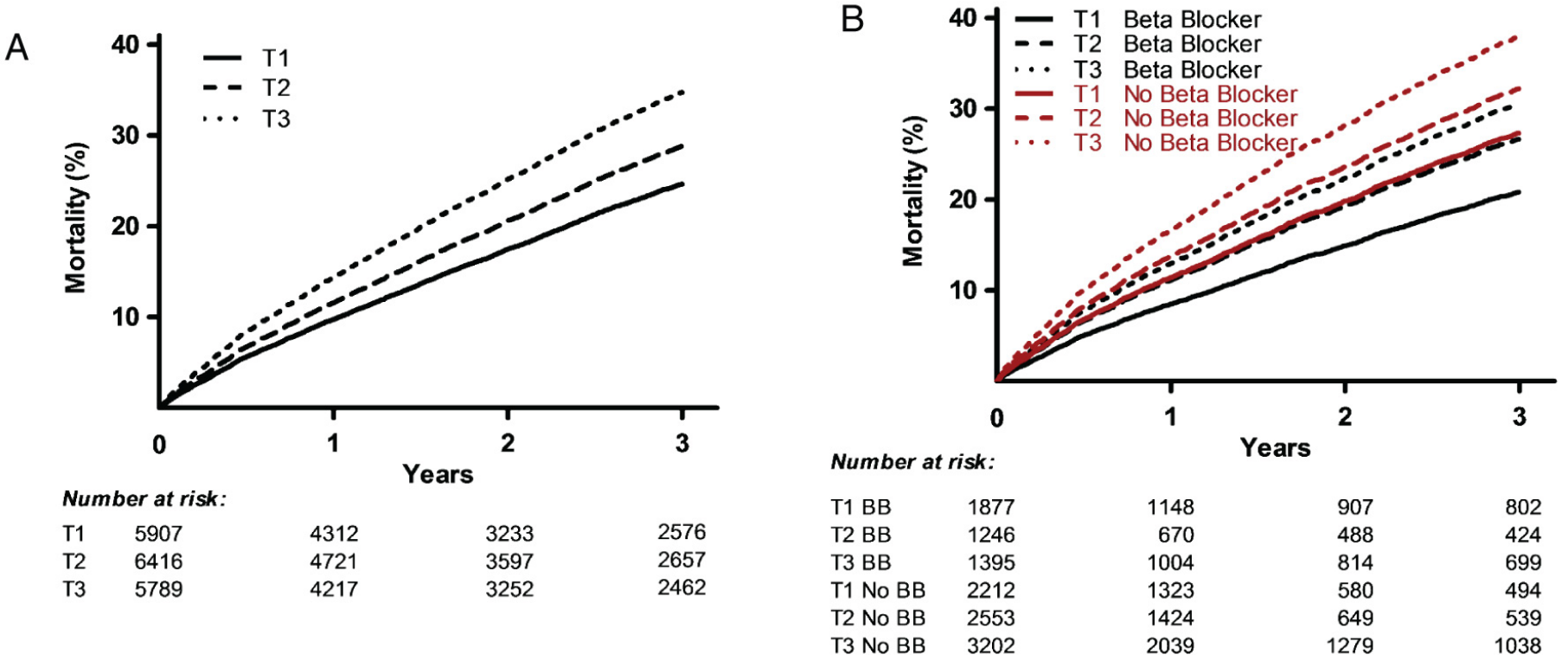
Table 2 Rate control target and drug therapy at the end of the dose-adjustment phase, according to treatment group

	Lenient rate control (n = 138)	Strict rate control (n = 149)	P-value
Rate control target or targets achieved, n (%)	134 (97.1)	108 (72.5)	<0.001
Resting heart rate, n (%)			
<70 b.p.m.	1 (0.7)	33 (22.1)	<0.001
70–80 b.p.m.	3 (2.2)	87 (58.4)	<0.001
80–90 b.p.m.	47 (34.1)	13 (8.7)	<0.001
90–100 b.p.m.	51 (37.0)	9 (6.0)	<0.001
>100 b.p.m.	36 (26.1)	7 (4.7)	<0.001
Heart rate at 1 year	84 ± 13	76 ± 12	<0.001
Heart rate at 2 years	83 ± 13	75 ± 12	<0.001
Heart rate at end of study	85 ± 14	76 ± 15	<0.001
Resting heart rate target achieved, n (%)	134 (97.1)	120 (80.5)	<0.001

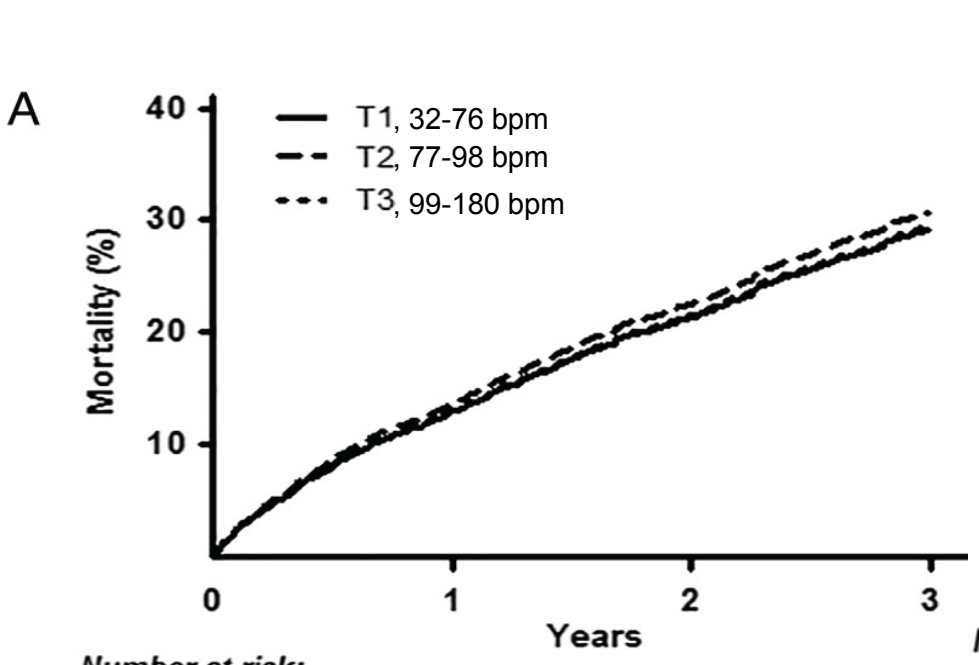
Survival analysis in patients in sinus rhythm according to baseline heart rate. Results from the MAGGIC meta-analysis



T1 ≤ 77 bpm
T2 78-98 bpm
T3 > 98 bpm

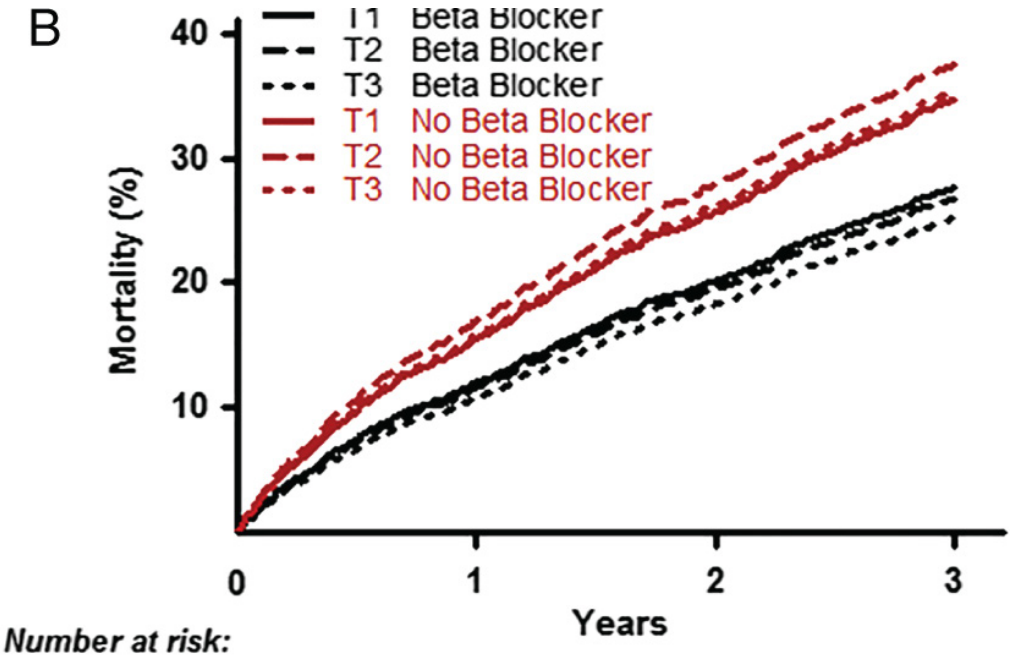
Simpson et al. European Journal of Heart Failure; 2015; 17:1182-1191.

Survival analysis in patients with atrial fibrillation (AF) according to baseline heart rate. Results from the MAGGIC meta-analysis



Number at risk:

T1	1031	560	381	312
T2	1019	589	373	312
T3	1061	785	613	509



Number at risk:

T1 BB	344	198	162	132
T2 BB	311	192	164	136
T3 BB	407	323	280	247
T1 No BB	617	309	176	142
T2 No BB	651	356	177	146
T3 No BB	603	426	301	240

Simpson et al. European Journal of Heart Failure; 2015; 17:1182-1191.

Take-home messages

- La tachicardiomiopatia è una condizione frequente con la FA come principale causa
- Va considerata soprattutto in pazienti con FA e IC di recente insorgenza senza altra causa nota
- L'IC è, per definizione, almeno parzialmente reversibile dopo trattamento dell'aritmia
- In caso di FA, non sono stai dimostrati benefici con terapia medica con una strategia di controllo del ritmo rispetto al controllo della frequenza cardiaca
- La terapia elettrica può dare risultati migliori soprattutto se eseguita precocemente
- E' auspicabile un controllo della frequenza cardiaca su valori $\leq$90/min