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Citta' della Salute e della Scienza
Molinette – Torino

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CREDITI ECM
Il corso ha ottenuto nr. 7 crediti ECM per Medico Chirurgo, Specialità: Cardiologia, Geriatria, Medicina Interna, MMG, Medicina di Urgenza
OBIETTIVO FORMATIVO.
Epidemiologia – Prevenzione e promozione della salute con acquisizione di nozioni tecnico-strumentali

CON IL CONTRIBUTO INCONDIZIONATO DI

BAYER

LA FIBRILLAZIONE ATRIALE E LA TERAPIA ANTICOAGULANTE NELL'ANZIANO

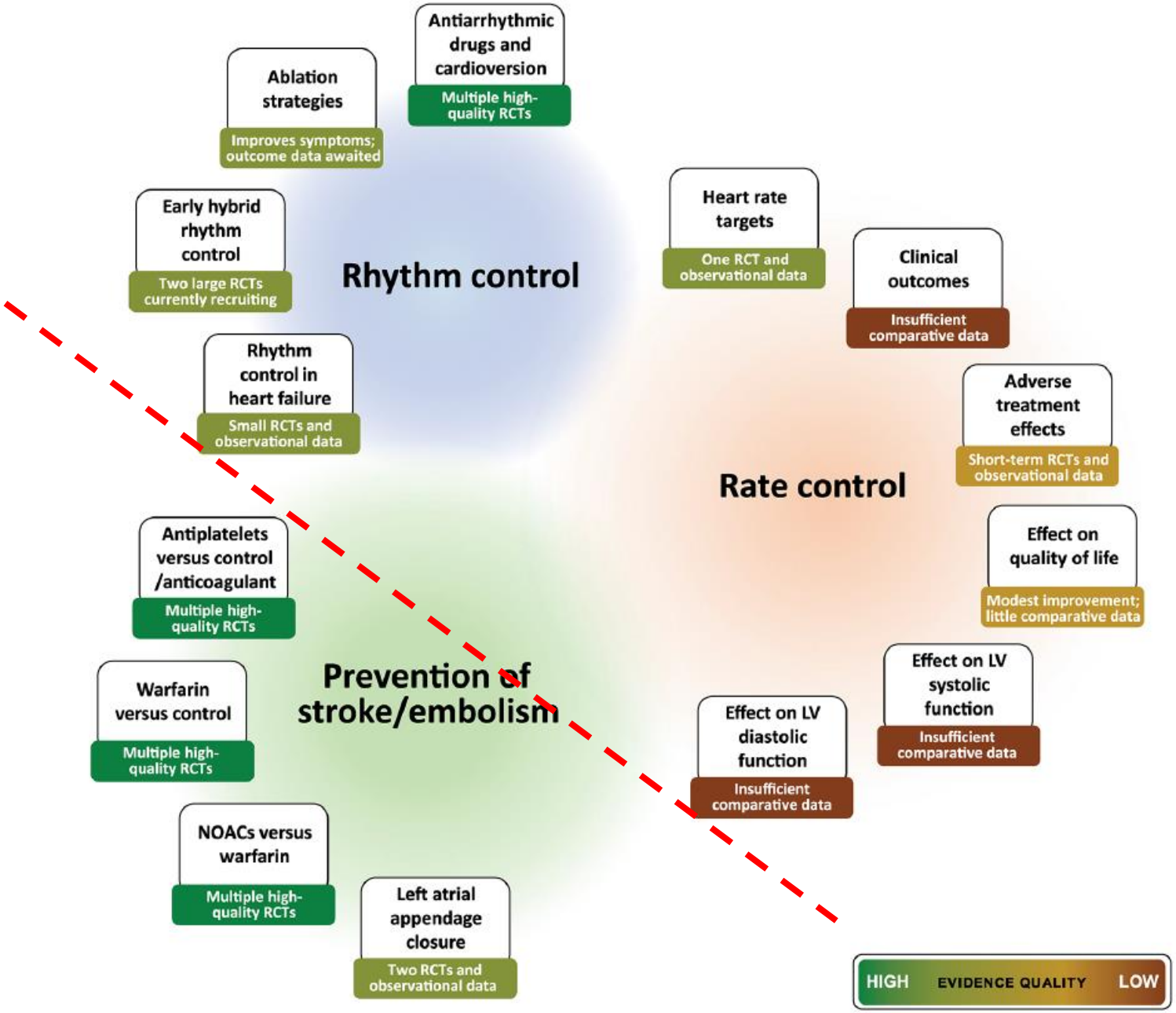
2/3 MARZO 2018
POLLENZO
ALBERGO DELL'AGENZIA - VIA FOSSANO, 21

La terapia non anticoagulante nel paziente con FA secondo le Linee Guida

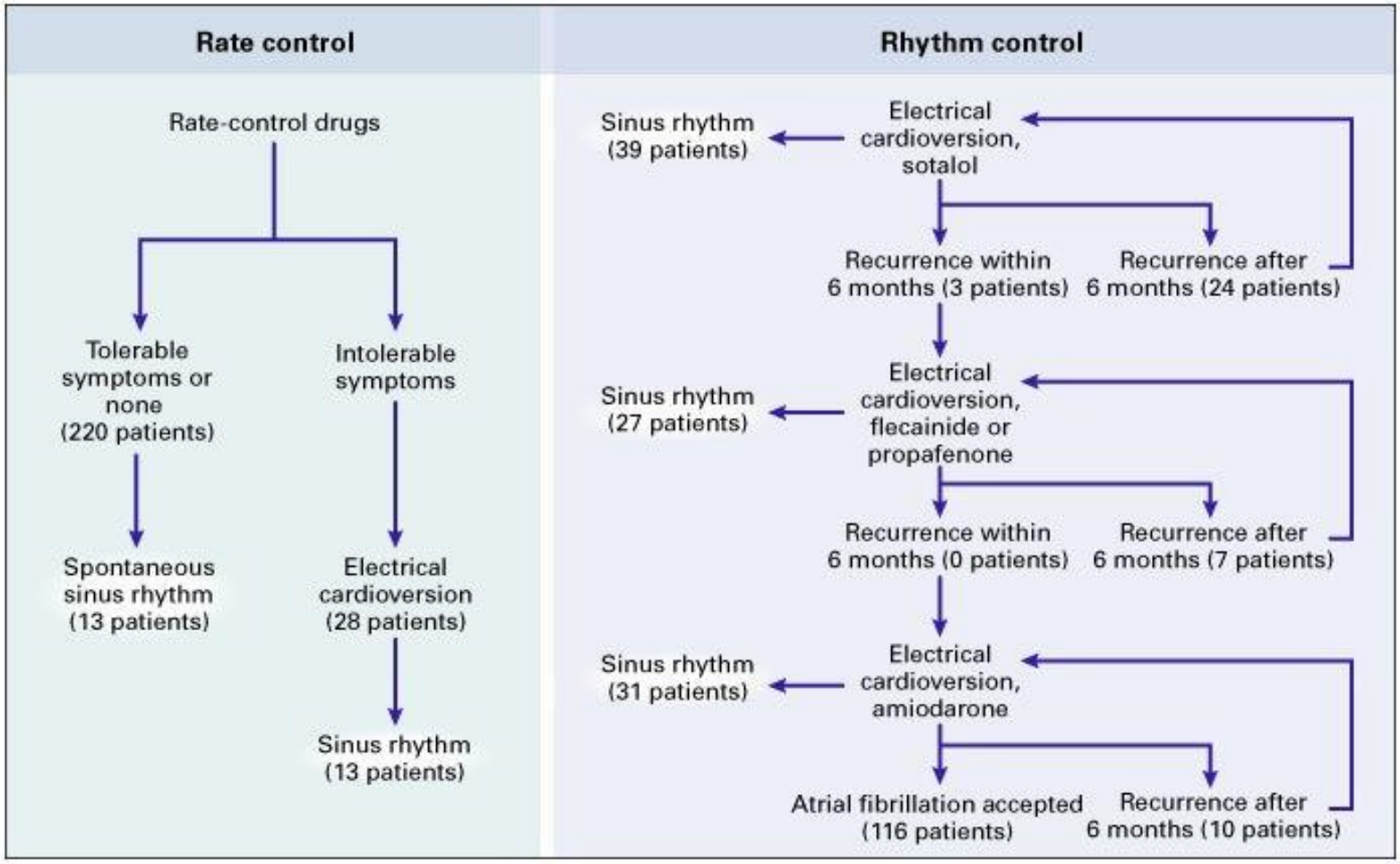
F. CONROTTO

SALUS SCIENTIA
AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

Rhythm or rate control strategy?

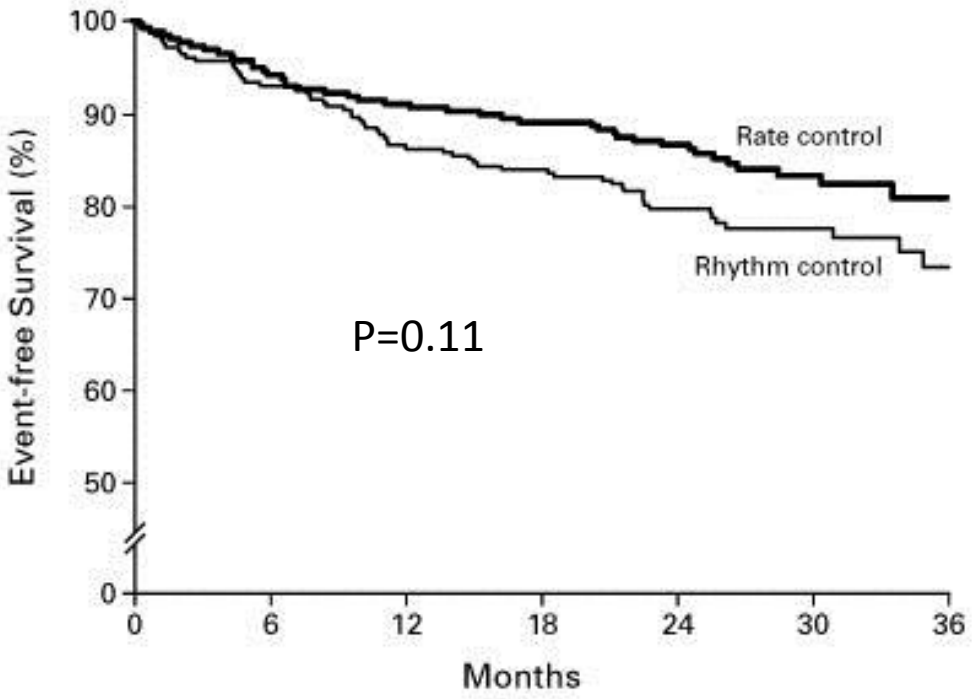

Antiarrhythmic drugs and cardioversion
Multiple high-quality RCTs
Ablation strategies
Improves symptoms; outcome data awaited
Early hybrid rhythm control
Two large RCTs currently recruiting
Rhythm control
Rhythm control in heart failure
Small RCTs and observational data
Heart rate targets
One RCT and observational data
Clinical outcomes
Insufficient comparative data
Adverse treatment effects
Short-term RCTs and observational data
Rate control
Effect on quality of life
Modest improvement; little comparative data
Antiplatelets versus control /anticoagulant
Multiple high-quality RCTs
Warfarin versus control
Multiple high-quality RCTs
Prevention of stroke/embolism
Effect on LV systolic function
Insufficient comparative data
Effect on LV diastolic function
Insufficient comparative data
NOACs versus warfarin
Multiple high-quality RCTs
Left atrial appendage closure
Two RCTs and observational data
HIGH
EVIDENCE QUALITY
LOW

Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation (RACE)



N Engl J Med 2002;347:1834–40

Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation (RACE)



No. at Risk							
Rate control	256	239	232	222	212	99	25
Rhythm control	266	243	224	218	207	85	24

N Engl J Med 2002;347:1834–40

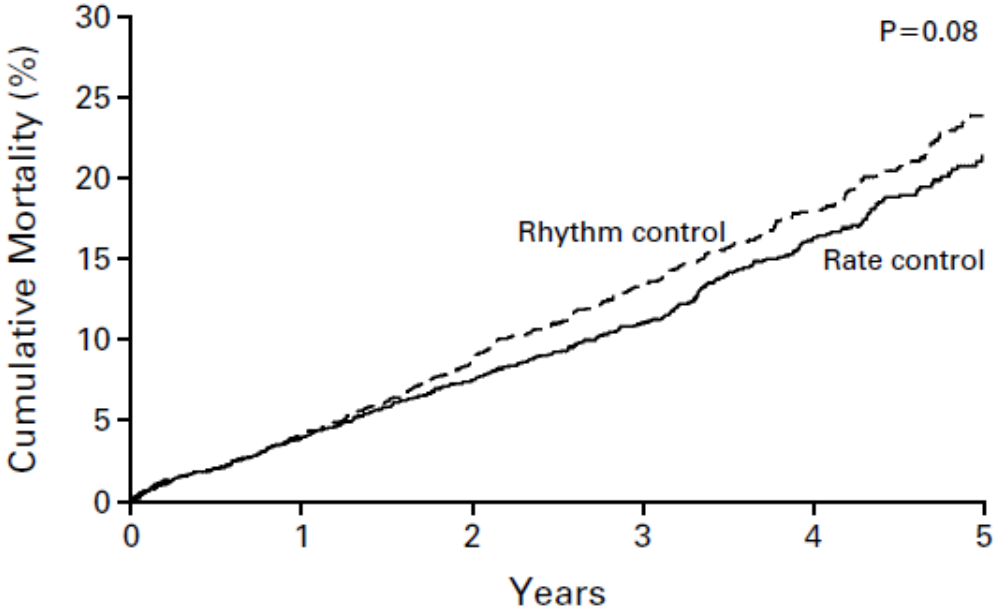
Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)

TABLE 1. BASE-LINE CHARACTERISTICS OF THE PATIENTS.*

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

N Engl J Med 2002;347:1825–33.

Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)



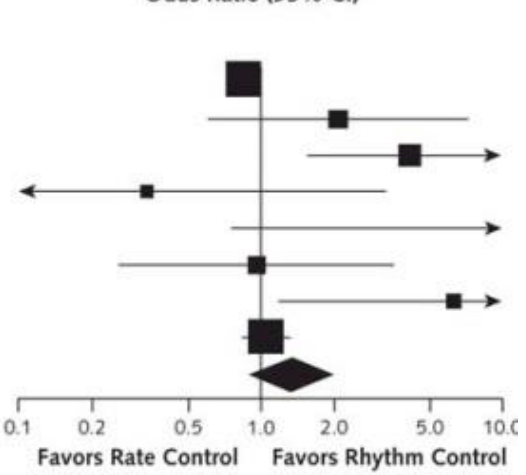
No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

N Engl J Med 2002;347:1825–33.

Rate- and Rhythm-Control Therapies in Patients With Atrial Fibrillation: A Systematic Review

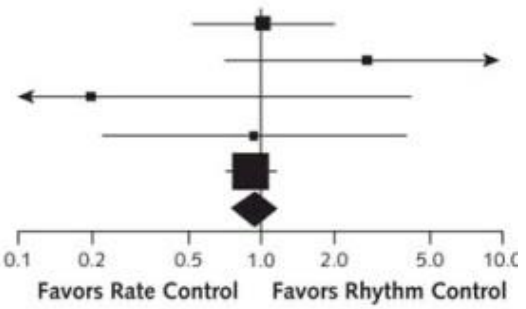
A.

Study, Year (Reference)	Odds Ratio (95% CI)	Deaths/Total, *n/N*	
		Rate Control	Rhythm Control
Wyse et al, 2002 (27)	0.851 (0.720–1.005)	310/2027	356/2033
Carlsson et al, 2003 (18)	2.087 (0.608–7.167)	8/100	4/100
Okçün et al, 2004 (20)	4.125 (1.562–10.895)	36/84	6/39
Opolski et al, 2004 (21)	0.337 (0.034–3.291)	1/101	3/104
Vora et al, 2004 (26)	14.099 (0.754–263.543)	5/40	0/45
Petrac et al, 2005 (22)	0.957 (0.260–3.532)	5/52	5/50
Yildiz et al, 2008 (28)	6.270 (1.185–33.192)	5/66	2/155
Talajic et al, 2010 (24)	1.048 (0.836–1.314)	228/694	217/682
Overall	1.343 (0.893–2.020)		



B.

		Cardiovascular Deaths/Total, *n/N*	
		Rate Control	Rhythm Control
Van Gelder et al, 2002 (25)	1.042 (0.529–2.051)	18/256	18/266
Carlsson et al, 2003 (18)	2.812 (0.724–10.924)	8/100	3/100
Opolski et al, 2004 (21)	0.202 (0.010–4.259)	0/101	2/104
Petrac et al, 2005 (22)	0.958 (0.226–4.060)	4/52	4/50
Talajic et al, 2010 (24)	0.926 (0.728–1.179)	175/694	182/682
Overall	0.959 (0.769–1.196)		

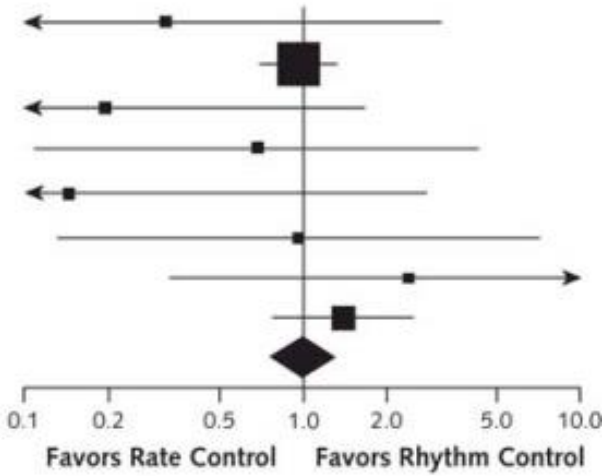


Ann Intern Med. 2014;160(11):760-773.

Rate- and Rhythm-Control Therapies in Patients With Atrial Fibrillation: A Systematic Review

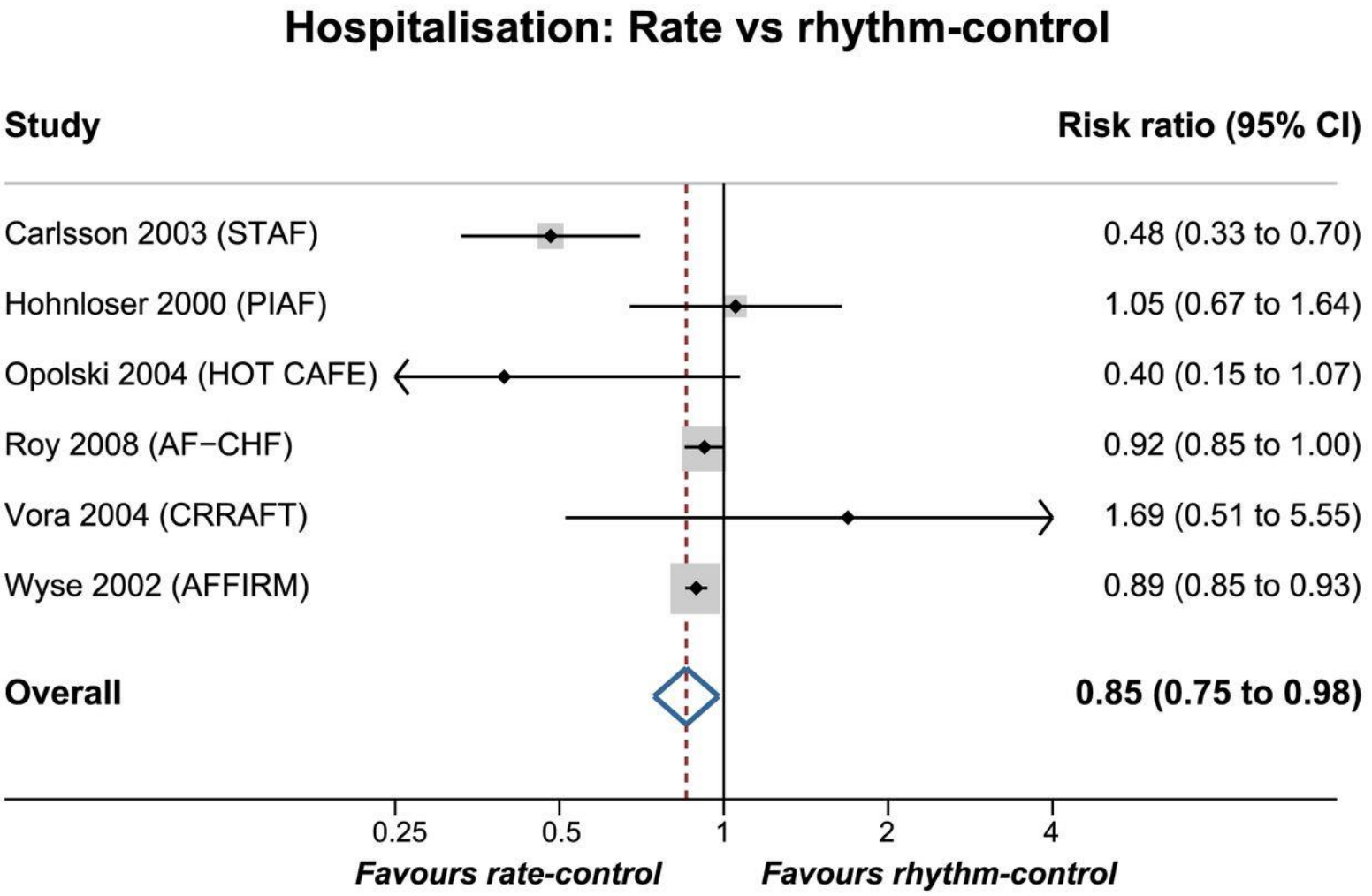
C.

		Stroke/Total, *n/N*	
		Rate Control	Rhythm Control
Brignole et al, 2002 (17)	0.319 (0.032–3.142)	1/69	3/68
Wyse et al, 2002 (27)	0.964 (0.701–1.326)	77/2027	80/2033
Carlsson et al, 2003 (18)	0.192 (0.022–1.673)	1/100	5/100
Okçün et al, 2004 (20)	0.685 (0.110–4.276)	3/84	2/39
Opolski et al, 2004 (21)	0.143 (0.007–2.801)	0/101	3/104
Petrac et al, 2005 (22)	0.960 (0.130–7.091)	2/52	2/50
Yildiz et al, 2008 (28)	2.391 (0.330–17.342)	2/66	2/155
Talajic et al, 2010 (24)	1.392 (0.776–2.495)	28/694	20/682
Overall	0.994 (0.759–1.302)		



Ann Intern Med. 2014;160(11):760-773.

A review of rate control in atrial fibrillation, and the rationale and protocol for the RATE-AF trial

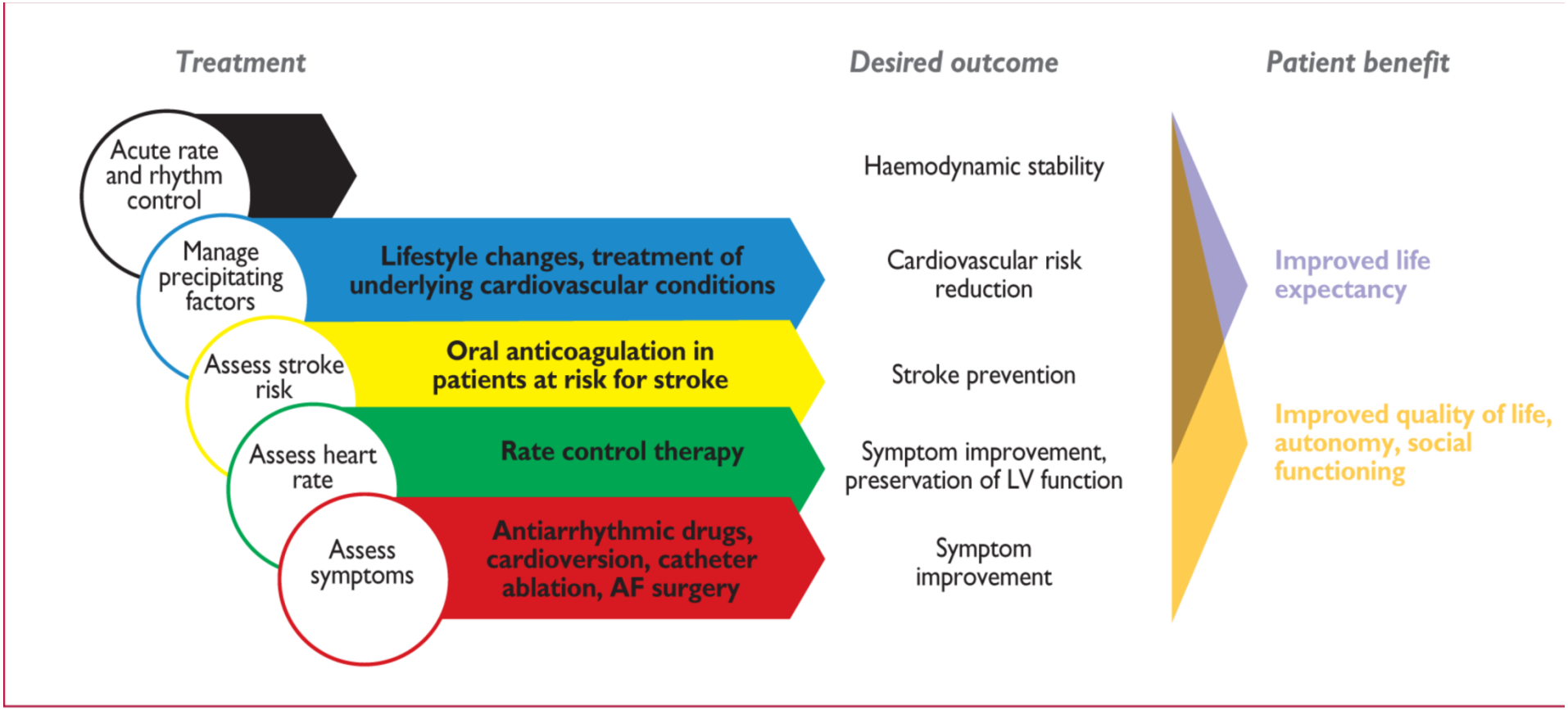


BMJ Open 2017

Although many clinicians believe that maintaining sinus rhythm can improve outcomes in AF patients, all trials that have compared rhythm control and rate control to rate control alone (with appropriate anticoagulation) have resulted in neutral outcomes.

For now, rhythm control therapy is indicated to improve symptoms in AF patients who remain symptomatic on adequate rate control therapy.

From: 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS
Eur Heart J. 2016;37(38):2893-2962. doi:10.1093/eurheartj/ehw210

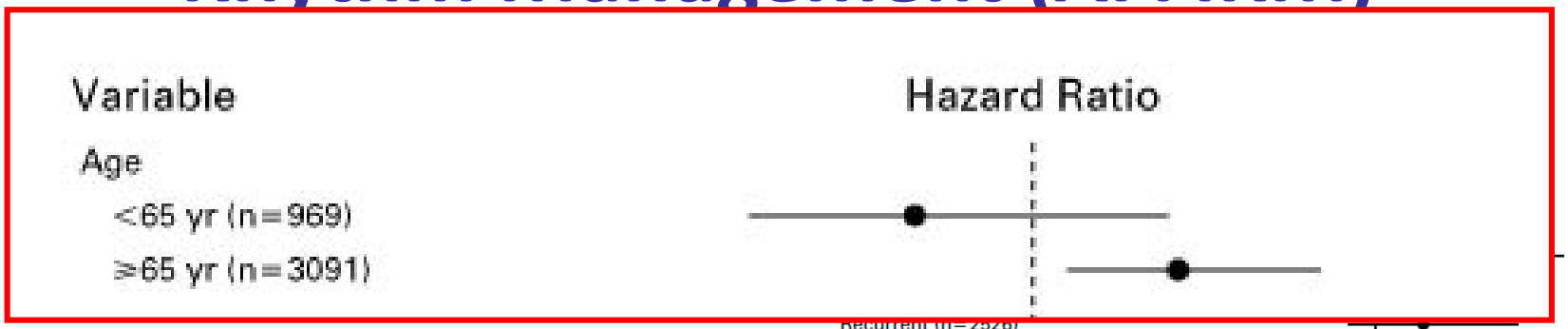


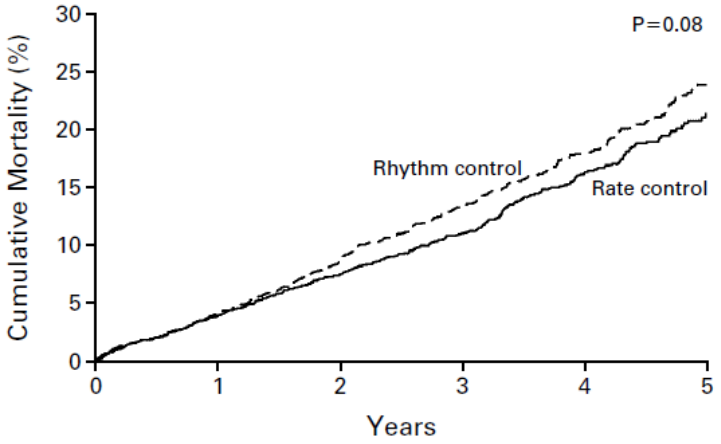
AF = atrial fibrillation; LV = left ventricular.

From: 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

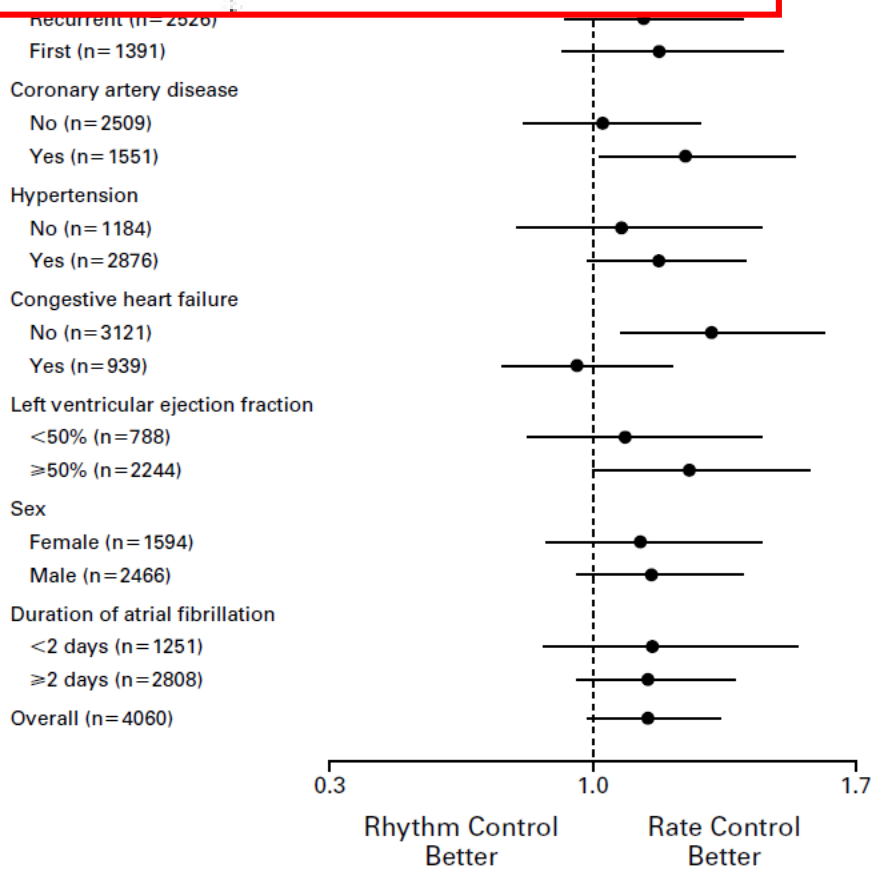
Eur Heart J. 2016;37(38):2893-2962. doi:10.1093/eurheartj/ehw210

Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)



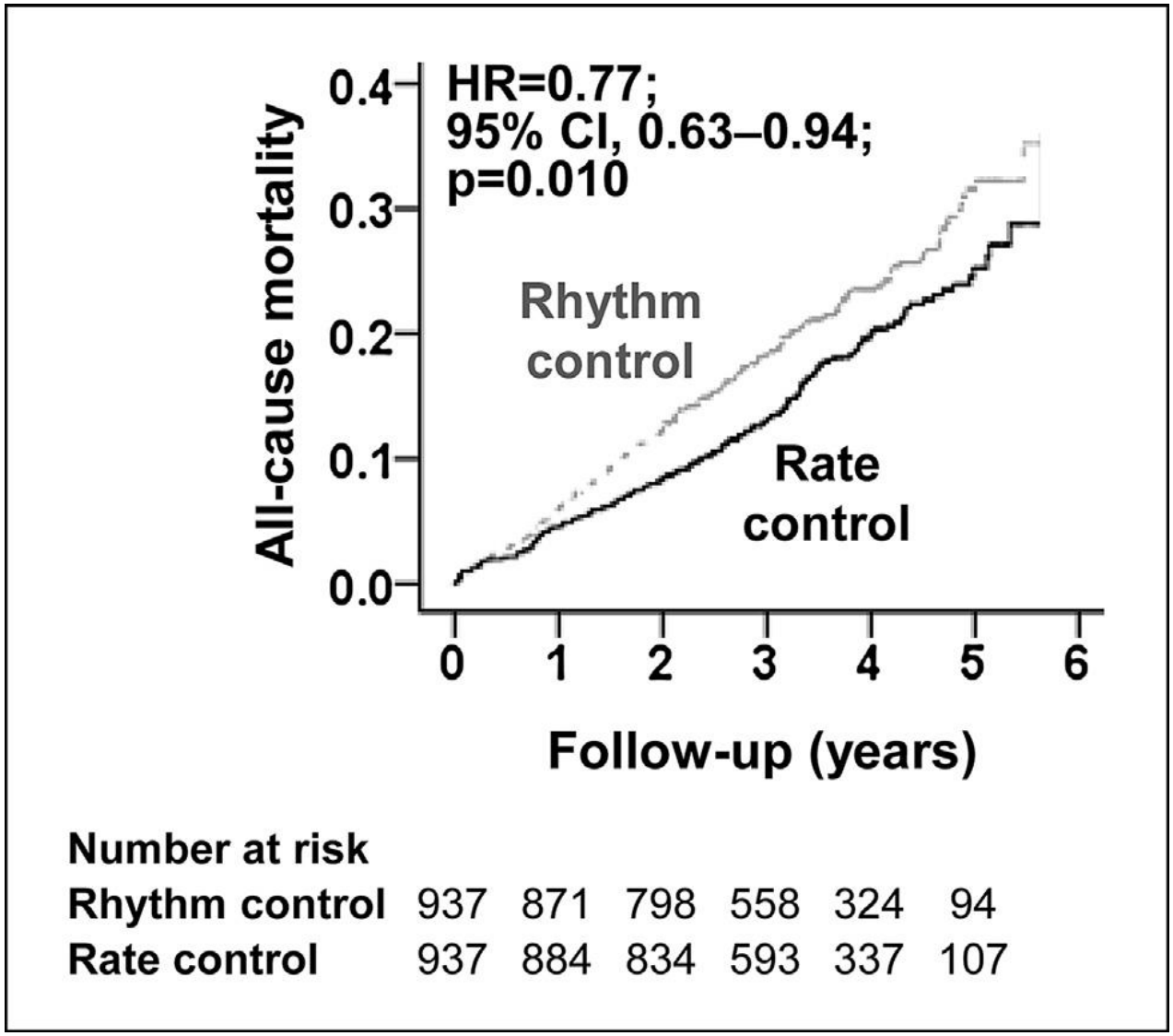


No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)



N Engl J Med 2002;347:1825–33.

Rate-control versus Rhythm-control Strategies and Outcomes in Septuagenarians with Atrial Fibrillation



The American Journal of Medicine (2013) 126, 887-893

Rate-control versus Rhythm-control Strategies and Outcomes in Septuagenarians with Atrial Fibrillation

Table 3 Other Outcomes among the Subset of AFFIRM Patients Aged 70-80 Years with Atrial Fibrillation

Outcomes	Events (%)				
	Rate-control strategy (n = 937)	Rhythm-control Strategy (n = 937)	Absolute Risk Difference*	Hazard Ratio (95% CI)	*P* Value
Cardiovascular mortality	84 (9%)	92 (10%)	1%	0.88 (0.65-1.18)	.39
Due to cardiac causes	65 (7%)	74 (8%)	1%	0.85 (0.61-1.18)	.33
Arrhythmic	35 (4%)	45 (5%)	1%	0.75 (0.48-1.16)	.20
Nonarrhythmic	30 (3%)	29 (3%)	0%	1.00 (0.60-1.66)	1.00
Due to vascular causes	19 (2%)	18 (2%)	0%	1.01 (0.53-1.93)	.97
Noncardiovascular mortality	70 (8%)	108 (12%)	4%	0.62 (0.46-0.84)	.002
All-cause hospitalization	571 (61%)	641 (68%)	7%	0.76 (0.68-0.86)	<.001
Cardiovascular	288 (31%)	387 (41%)	10%	0.66 (0.56-0.77)	<.001
Noncardiovascular	283 (30%)	254 (27%)	3%	1.07 (0.91-1.27)	.42
Stroke	41 (4%)	44 (5%)	1%	0.90 (0.59-1.37)	.61
Major bleeding†	78 (8%)	72 (8%)	0%	1.05 (0.77-1.45)	.75

The American Journal of Medicine (2013) 126, 887-893

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Risk of Proarrhythmic Events in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study

A Multivariate Analysis

Elizabeth S. Kaufman, MD, FACC,* Paul A. Zimmermann, MD, FACC,† Ted Wang, MD, FACC,‡
George W. Dennish III, MD, FACC,§ Patrick D. Barrell, BS,‖ Mary L. Chandler, MD, FACOG,‖
H.
Cle

After multivariate adjustment he predictors of ventricular proarrhythmic events in all patients were:
age (HR 1.96, p 0.03)
history of congestive heart failure (HR 2.68, p 0.0001),
and mitral regurgitation 2/4 (HR 2.04, p 0.003).

calculated.

RESULTS A total of 2,033 patients received 3,030 exposures to antiarrhythmic drugs. Ninety-six arrhythmic events occurred by six years. Patients with a left ventricular ejection fraction <40% had more arrhythmic events. Twelve documented cases of torsade de pointes VT were noted. The incidence of torsade de pointes was 0.6% at five years (95% confidence interval 0.32 to 1.07).

CONCLUSIONS The overall risk of adverse arrhythmic events upon exposure to antiarrhythmic drugs in the AFFIRM study was reasonably low. Strict criteria for the safe use of antiarrhythmic drugs were successful in minimizing proarrhythmic events. (J Am Coll Cardiol 2004;44: 1276–82) © 2004 by the American College of Cardiology Foundation

ESC
European Society of Cardiology

EHRA POSITION PAPER

Pharmacokinetics alterations in elderly

PK component	Physiological change	Effect
Absorption	Reduced gastric acid Reduced gastric emptying rate Reduced GI motility Reduced GI blood flow Reduced absorptive surface	Reduced tablet dissolution Reduced solubility for basic drugs Decreased absorption of acid drugs Less drug absorption
Distribution	Decreased body mass Increased body fat Decreased proportion of body water Decreased plasma albumin	Increased Vd of lipid soluble drugs Decrease Vd of water-soluble drugs Changed proportion of free drug
Metabolism	Reduced liver mass Reduced liver blood flow Reduced liver metabolism rate/capacity	Accumulation of metabolized drugs
Excretion	Reduced glomerular filtration Reduced renal tubular function Reduced renal blood flow	Accumulation of renal cleared drugs

Relationships Between Sinus Rhythm, Treatment, and Survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study

The AFFIRM Investigators*

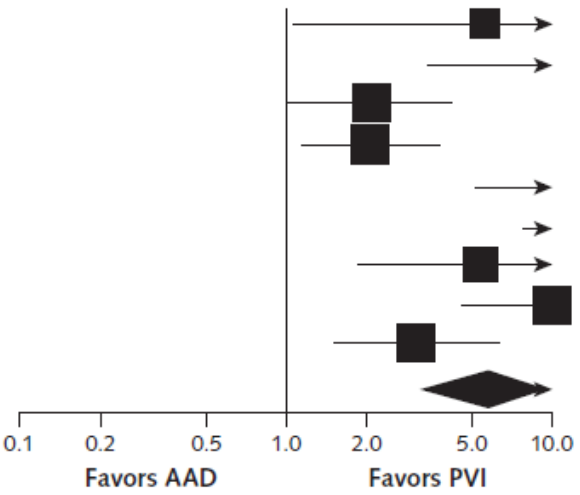
Background—The AFFIRM Study showed that treatment of patients with atrial fibrillation and a high risk for stroke or death with a rhythm-control strategy offered no survival advantage over a rate-control strategy in an intention-to-treat analysis. This article reports an "on-treatment" analysis of the relationship of survival to cardiac rhythm and treatment as they changed over time.

Conclusions—Warfarin use improves survival. SR is either an important determinant of survival or a marker for other factors associated with survival that were not recorded, determined, or included in the survival model. Currently available AADs are not associated with improved survival, which suggests that any beneficial antiarrhythmic effects of AADs are offset by their adverse effects. If an effective method for maintaining SR with fewer adverse effects were available, it might be beneficial.

(*Circulation*. 2004;109:1509-1513.)

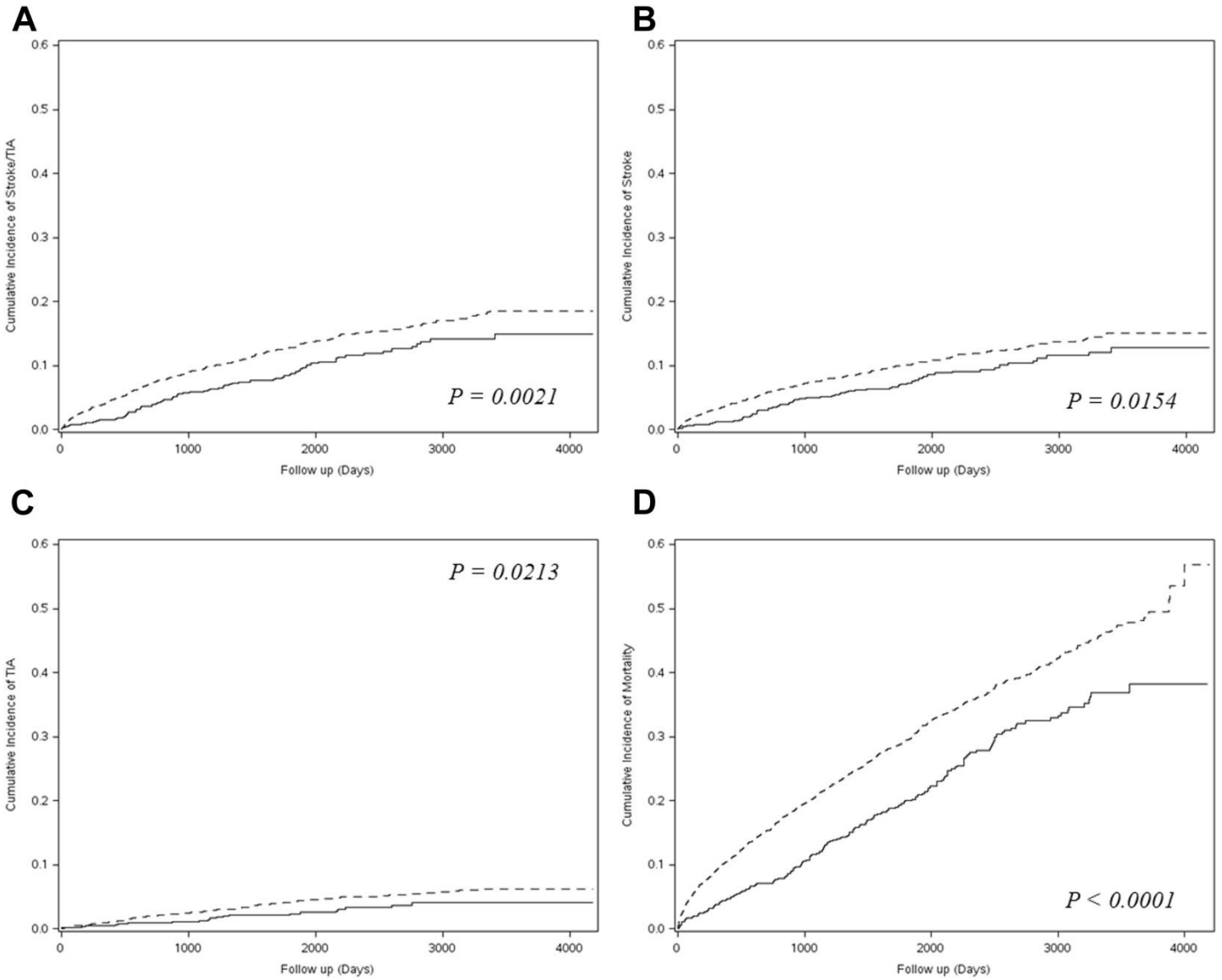
Rate- and Rhythm-Control Therapies in Patients With Atrial Fibrillation: A Systematic Review

Study, Year (Reference)	Odds Ratio (95% CI)	Maintenance of Sinus Rhythm/Total, *n/N*	
		PVI	AAD
Krittayaphong et al, 2003 (147)	5.500 (1.065–28.416)	11/14	6/15
Wazni et al, 2005 (157)	11.846 (3.387–41.433)	28/32	13/35
Oral et al, 2006 (114)	2.066 (1.028–4.155)	57/77	40/69
Pappone et al, 2006 (115)	2.048 (1.130–3.711)	72/99	56/99
Stabile et al, 2006 (119)	13.300 (5.069–34.894)	38/68	6/69
Jaïs et al, 2008 (143)	24.769 (8.634–71.059)	46/52	13/55
Forleo et al, 2009 (112)	5.333 (1.839–15.471)	28/35	15/35
Wilber et al, 2010 (126)	9.917 (4.509–21.808)	70/106	10/61
Mont et al, 2014 (132)	3.059 (1.494–6.263)	69/98	21/48
Overall	5.874 (3.180–10.849)		



Ann Intern Med. 2014;160(11):760-773.

Catheter ablation of atrial fibrillation is associated with reduced risk of stroke and mortality: A propensity score–matched analysis

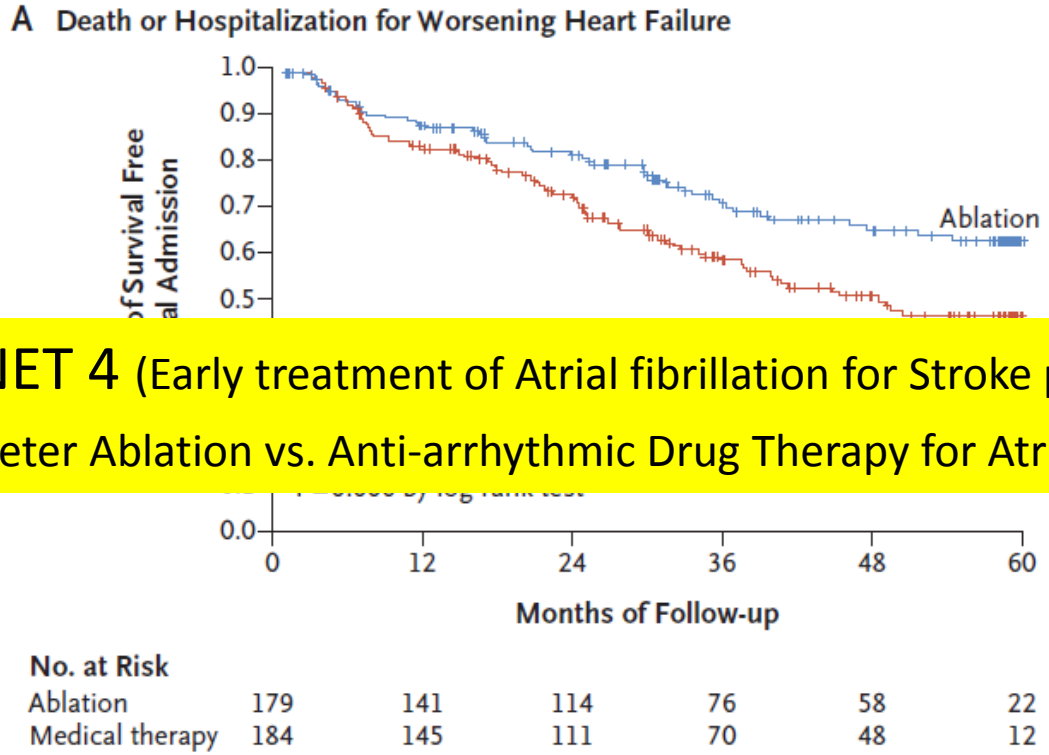


Heart Rhythm 2017;14:635–642

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 1, 2018 VOL. 378 NO. 5

Catheter Ablation for Atrial Fibrillation with Heart Failure



EAST – AFNET 4 (Early treatment of Atrial fibrillation for Stroke prevention Trial)

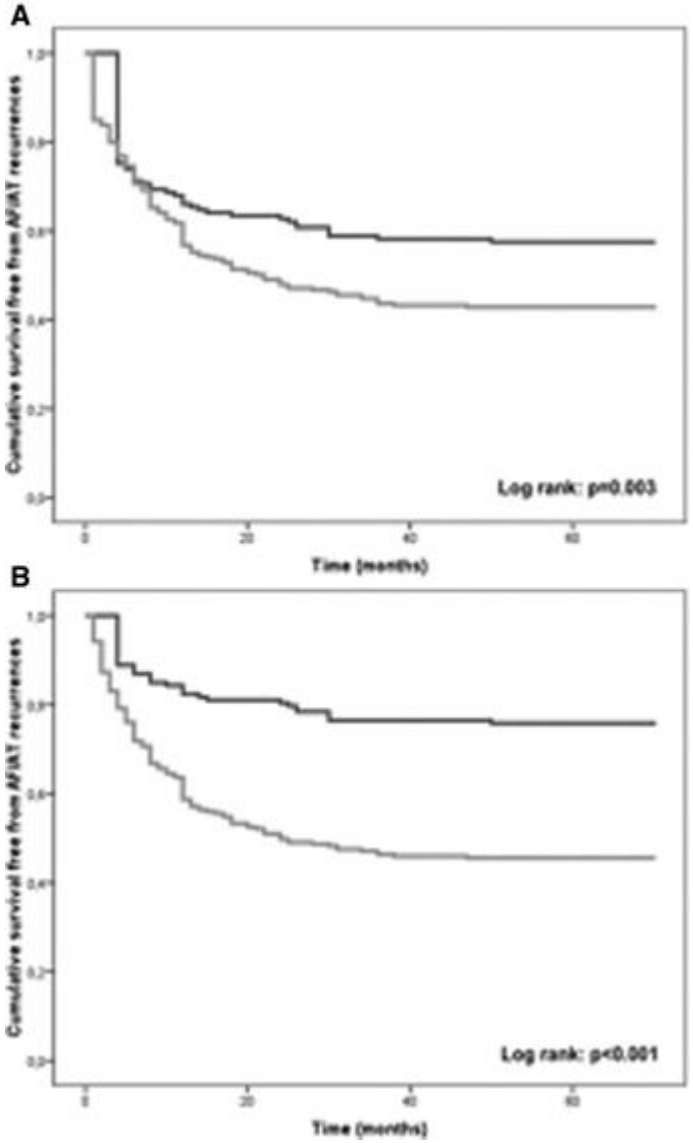
CABANA (Catheter Ablation vs. Anti-arrhythmic Drug Therapy for Atrial Fibrillation Trial)

Clinical management of arrhythmias in elderly patients: results of the European Heart Rhythm Association survey

	75 years	80 years	85 years	None
Catheter ablation				
Supraventricular tachycardia	0	2.0	8.2	89.8
Ventricular arrhythmias	2.0	18.4	14.3	65.3
AF	32.6	34.7	14.3	18.4
Device implantation				
Pacemaker	0	0	0	100
CRT	0	8.3	20.8	70.8
ICD for primary prevention	18.4	32.6	30.6	18.4
ICD for secondary prevention	0	12.2	12.2	75.5

Europace 2015; 17: 314–317

Long-Term Efficacy and Safety of Two Different Rhythm Control Strategies in Elderly Patients with Symptomatic Persistent Atrial Fibrillation



Primary endopoint:
AF recurrences
(visits, ECG, ECG Holter)

Long-Term Efficacy and Safety of Two Different Rhythm Control Strategies in Elderly Patients with Symptomatic Persistent Atrial Fibrillation

Acute adverse event	Group A 181	Group B 293	P value
Stroke/TIA	6 (3.3%)	2(0.7%)	0.058
Pericardial effusion	3 (1.7%)	0	0.056
Bleedings	0	0	1

Long-Term Efficacy and Safety of Two Different Rhythm Control Strategies in Elderly Patients with Symptomatic Persistent Atrial Fibrillation

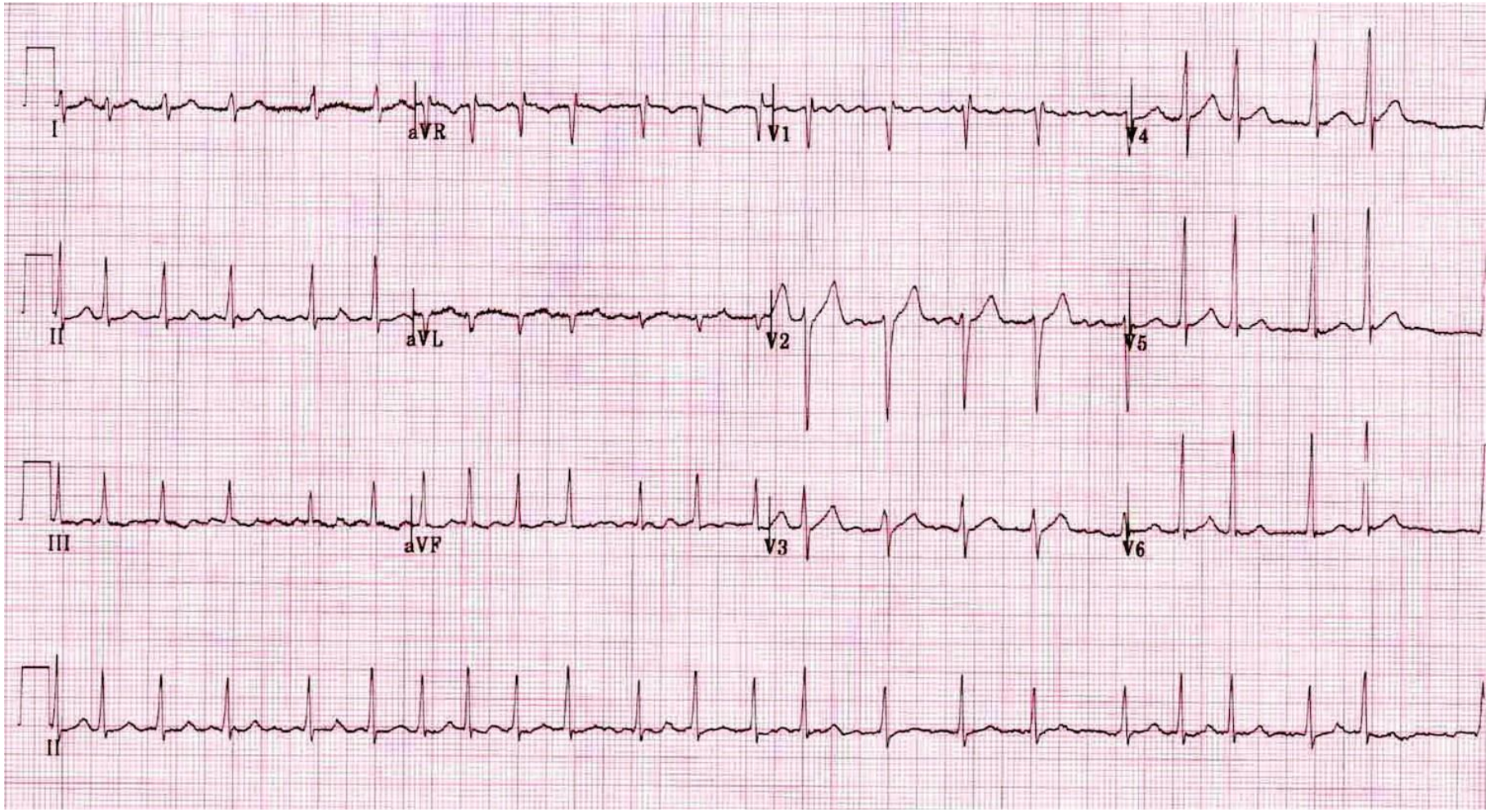
Long term AE	Group A 153	Group B 259	p value
Stroke/TIA	2 (1.3%)	5 (1.9 %)	0.714
Peripheral embolism	1 (0.6%)	1 (0.4%)	1
Minor bleedings	1 (0.6%)	12 (4.6%)	0.026
Major bleedings	2 (1.3%)	2 (0.8%)	0.629
AAD AE	4 (2.6%)	33 (12.7%)	< 0.001

Although the evidence base is smaller for other treatment options in AF, the available data support the use of available rate and rhythm control interventions, including pacemakers and catheter ablation, without justification to discriminate by age group

….

Impairment of renal and hepatic function and multiple simultaneous medications make drug interactions and adverse drug reactions more likely.

RATE CONTROL



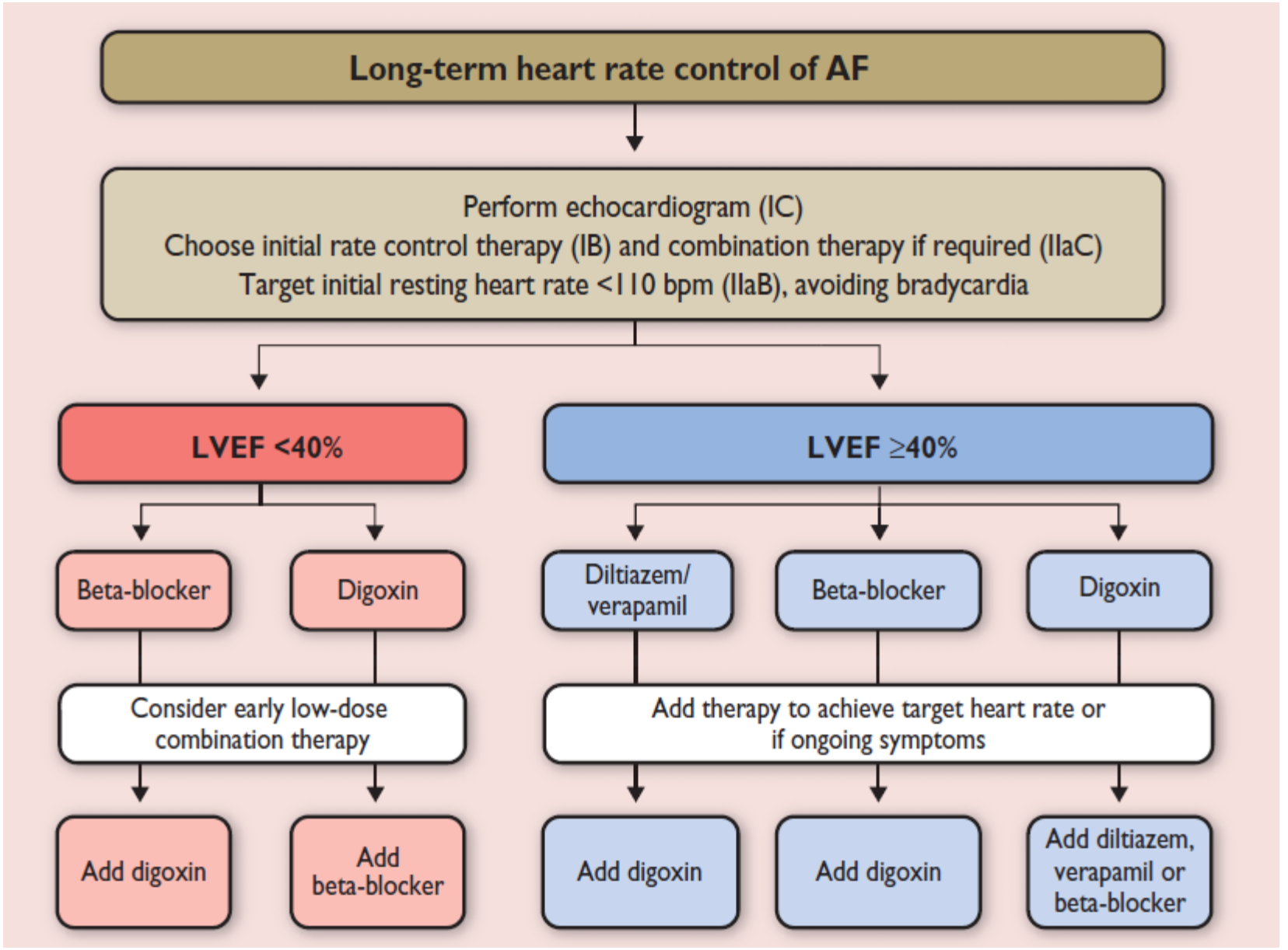
European Heart Journal (2016) 37, 2893–2962
doi:10.1093/eurheartj/ehw210

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

Acute rate control

- For acute rate control, beta-blockers and diltiazem or verapamil are preferred over digoxin because of their rapid onset of action and effectiveness at high sympathetic tone

- The choice of drug and target heart rate will depend on patient characteristics, symptoms, LVEF and haemodynamics, but a lenient initial approach to heart rate seems acceptable.


Long-term heart rate control of AF
Perform echocardiogram (IC)
Choose initial rate control therapy (IB) and combination therapy if required (IIaC)
Target initial resting heart rate <110 bpm (IIaB), avoiding bradycardia
LVEF <40%
LVEF ≥40%
Beta-blocker
Digoxin
Diltiazem/ verapamil
Beta-blocker
Digoxin
Consider early low-dose combination therapy
Add therapy to achieve target heart rate or if ongoing symptoms
Add digoxin
Add beta-blocker
Add digoxin
Add digoxin
Add diltiazem, verapamil or beta-blocker

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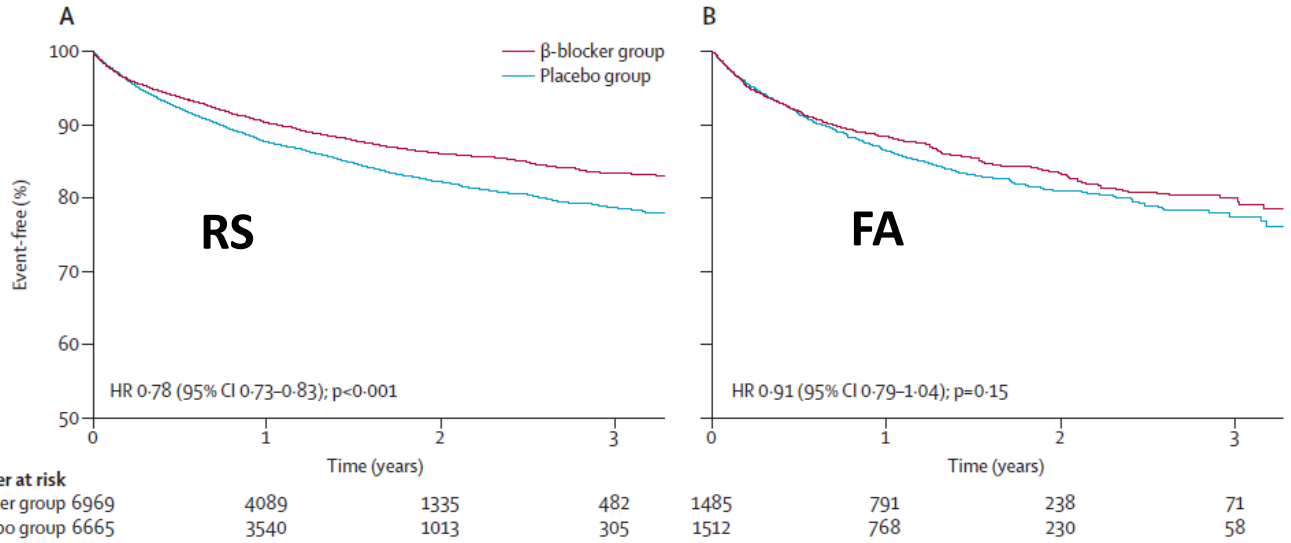
Beta blockers

This Task Force still considers beta-blockers as a useful first-line rate control agent across all AF patients, based on the potential for symptomatic and functional improvement as a result of rate control, the lack of harm from published studies, and the good tolerability profile across all ages in sinus rhythm and in AF.



Lancet 2014;384:2235–2243.

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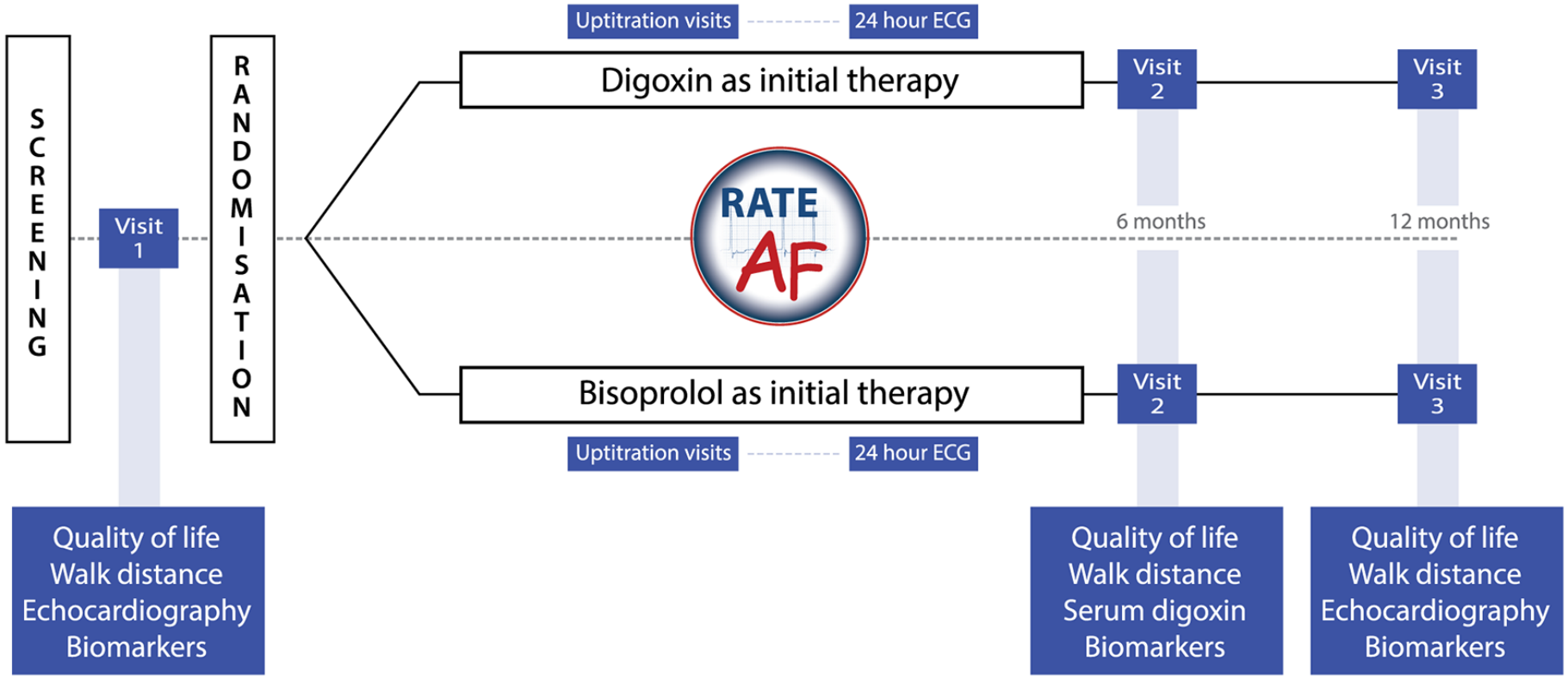
Digitalis

Lower doses of digoxin (≤250 mg once daily), corresponding to serum digoxin levels of 0.5–0.9 ng/mL

Table 3 Association of digoxin use as initial therapy at baseline with outcomes in a propensity-matched cohort of patients with atrial fibrillation enrolled in the AFFIRM trial

Post-match (n = 1756)	Events (%)		Hazard ratio (95% CI)	P-value
	Digoxin use as initial baseline therapy			
	No (n = 878) (%)	Yes (n = 878) (%)		
All-cause mortality[a]	118 (13)	124 (14)	1.06 (0.83–1.37)	0.640
Cardiovascular	56 (6)	63 (7)	1.13 (0.79–1.63)	0.494
Non-cardiovascular	48 (6)	51 (6)	1.08 (0.73–1.60)	0.709
All-cause hospitalization	516 (59)	495 (56)	0.96 (0.85–1.09)	0.510
Non-fatal arrhythmias[b]	10 (1)	9 (1)	0.90 (0.37–2.23)	0.827

RATE-AF trial



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ESC GUIDELINES

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Heart rate targets in atrial fibrillation

Lenient rate control (<110) is an acceptable initial approach, regardless of heart failure status, unless symptoms call for stricter rate control.

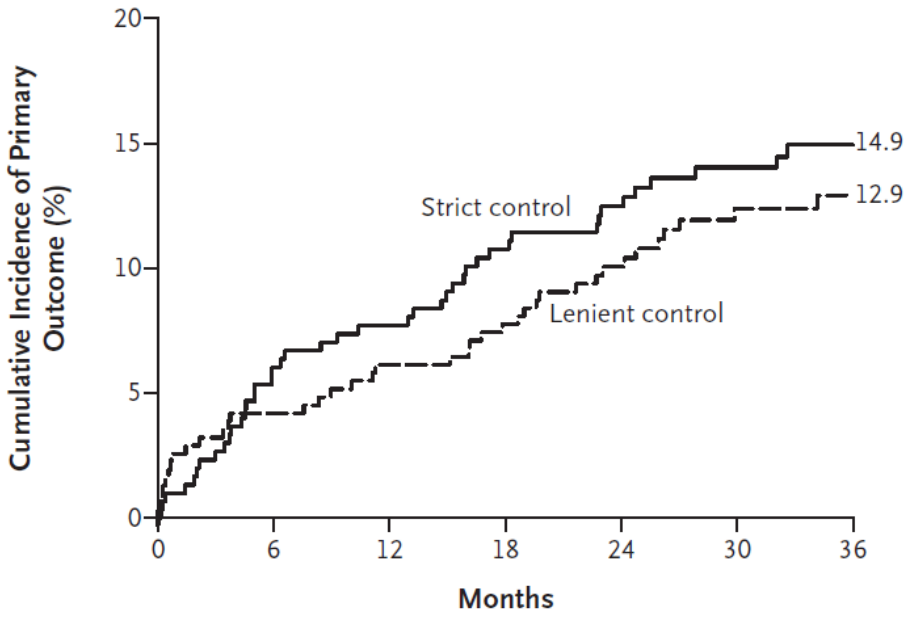
RACE (Rate Control Efficacy in Permanent Atrial Fibrillation) II

Lenient rate-control strategy

resting heart rate <110 beats per minute

Strict rate-control strategy

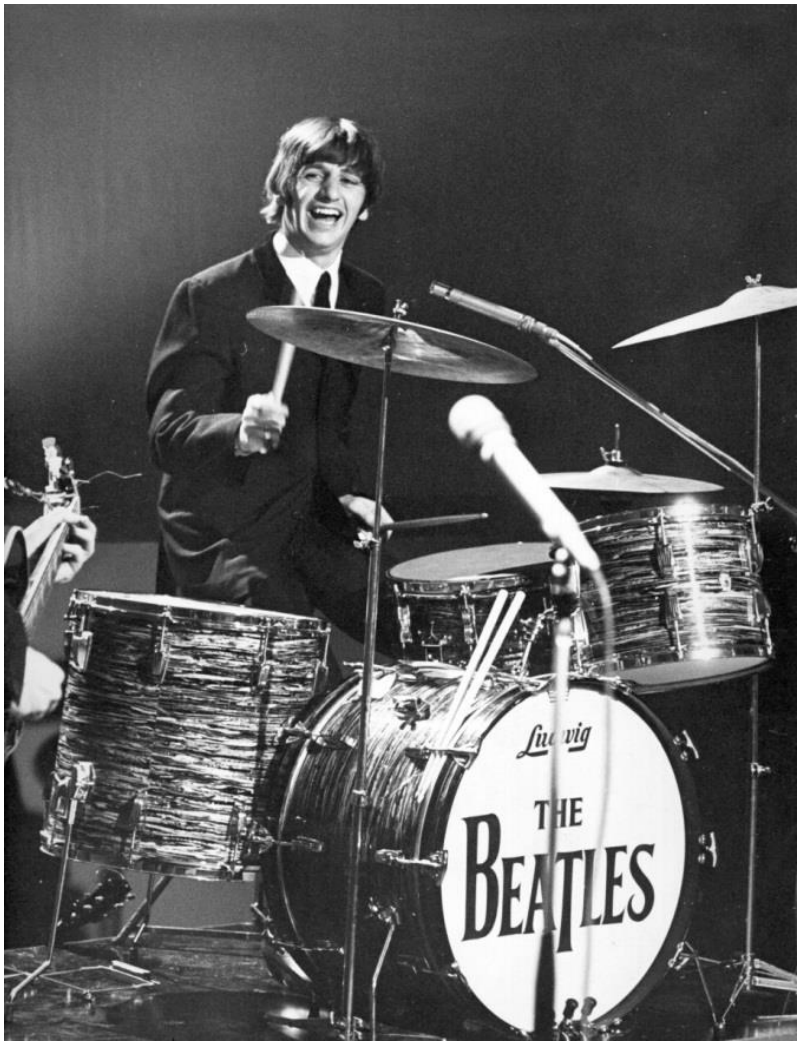
resting heart rate <80 beats per minute and heart rate during moderate exercise <110 beats per minute



No. at Risk							
Strict control	303	282	273	262	246	212	131
Lenient control	311	298	290	285	255	218	138

N Engl J Med 2010;362:1363–1373

Rhythm control



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Antiarrhythmic drugs for pharmacological cardioversion

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Drug	Route	1st dose	Follow-up dose	Risks	Reference
Flecainide	Oral IV	200–300 mg 1.5–2 mg/kg over 10 min	N/A	Hypotension, atrial flutter with 1:1 conduction, QT prolongation. Avoid in patients with IHD and/or significant structural heart disease.	595, 598
Amiodarone	IV[a]	5–7 mg/kg over 1–2 hours	50 mg/hour to a maximum of 1.0 g over 24 hours	Phlebitis, hypotension, bradycardia/AV block. Will slow ventricular rate. Delayed conversion to sinus rhythm (8–12 hours).	596–601
Propafenone	IV Oral	1.5–2 mg/kg over 10 min 450–600 mg		Hypotension, atrial flutter with 1:1 conduction, QRS prolongation (mild). Avoid in patients with IHD and/or significant structural heart disease.	622, 625
Ibutilide[b]	IV	1 mg over 10 min	1 mg over 10 min after waiting for 10 min	QT prolongation, polymorphic ventricular tachycardia/torsades de pointes (3–4% of patients). Will slow ventricular rate. Avoid in patients with QT prolongation, hypokalemia, severe LVH or low ejection fraction.	614, 615
Vernakalant	IV	3 mg/kg over 10 min	2 mg/kg over 10 min after waiting for 15 min	Hypotension, non-sustained ventricular arrhythmias, QT and QRS prolongation. Avoid in patients with SBP <100 mmHg, recent (<30 days) ACS, NYHA Class III and IV heart failure, QT interval prolongation (uncorrected QT >440 ms) and severe aortic stenosis.	602–605, 618

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ESC GUIDELINES

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Long-term anti arrhythmic drug therapy

(1) Treatment is aimed at reducing AF-related symptoms;
(2) Efficacy of antiarrhythmic drugs to maintain sinus rhythm is modest;
(3) Clinically successful antiarr[illegible]py may reduce rather than eliminate the re[illegible]
(4) If one antiarrhythm[illegible]fails', a clinically acceptable response may be achieved with another agent;
(5) Drug-induced pro-arrhythmia or extracardiac side-effects are frequent;
(6) Safety rather than efficacy considerations should primarily guide the choice of antiarrhythmic drug.

SAFETY FIRST

Drug	Dose	Main contra-indications and precautions	Warning signs warranting discontinuation	AV nodal slowing	Suggested ECG monitoring during initiation
Amiodarone	600 mg in divided doses for 4 weeks, 400 mg for 4 weeks, then 200 mg once daily	Caution when using concomitant therapy with QT-prolonging drugs and in patients with SAN or AV node and conduction disease. The dose of VKAs and of digitalis should be reduced. Increased risk of myopathy with statins. Caution in patients with pre-existing liver disease.	QT prolongation >500 ms	10–12 bpm in AF	Baseline, 1 week, 4 weeks
Dronedarone	400 mg twice daily	Contra-indicated in NYHA Class III or IV or unstable heart failure, during concomitant therapy with QT-prolonging drugs, or powerful CYP3A4 inhibitors (e.g. verapamil, diltiazem, azole antifungal agents), and when CrCl <30 ml/min. The dose of digitalis, beta-blockers, and of some statins should be reduced. Elevations in serum creatinine of 0.1–0.2 mg/dL are common and do not reflect a decline in renal function. Caution in patients with pre-existing liver disease.	QT prolongation >500 ms	10–12 bpm in AF	Baseline, 1 week, 4 weeks
Flecainide Flecainide slow release	100–150 mg twice daily 200 mg once daily	Contra-indicated if CrCl <50 mg/mL, liver disease, IHD or reduced LV ejection fraction. Caution in the presence of SAN or AV node or conduction disease. CYP2D6 inhibitors (e.g. fluoxetine or tricyclic antidepressants) increase plasma concentration.	QRS duration increases >25% above baseline	None	Baseline, day 1, day 2–3
Propafenone Propafenone SR	150–300 mg three times daily 225–425 mg twice daily	Contra-indicated in IHD or reduced LV ejection fraction. Caution in the presence of SAN or AV node and conduction disease, renal or liver impairment, and asthma. Increases concentration of digitalis and warfarin.	QRS duration increase >25% above baseline	Slight	Baseline, day 1, day 2–3
d,l sotalol	80–160 mg twice daily	Contra-indicated in the presence of significant LV hypertrophy, systolic heart failure, asthma, pre-existing QT prolongation, hypokalaemia, CrCl<50 mg/mL. Moderate renal dysfunction requires careful adaptation of dose.	QT interval >500 ms, QT prolongation by >60 ms upon therapy initiation	Similar to high dose blockers	Baseline, day 1, day 2–3

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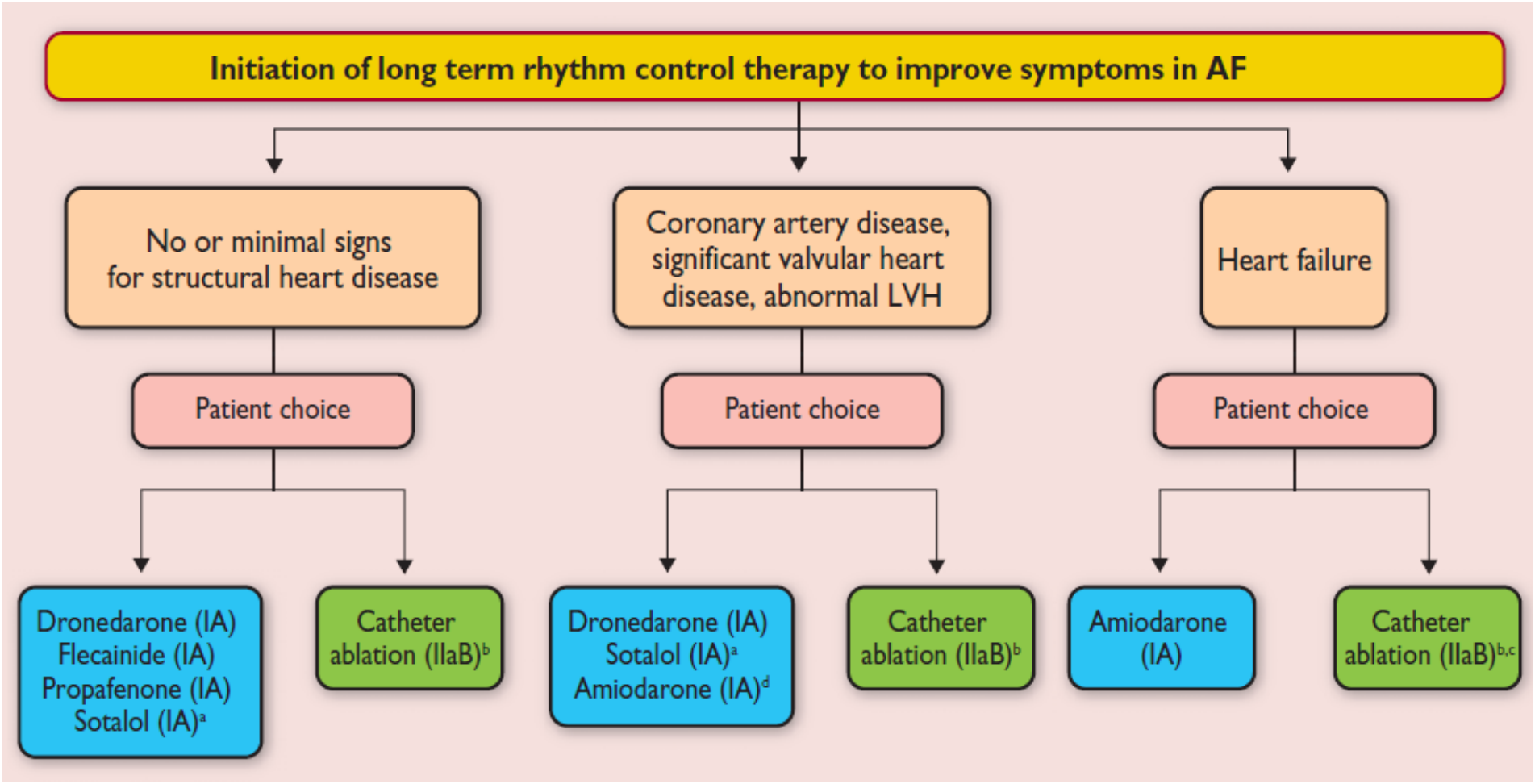

Conclusions

1) *rhythm control therapy is indicated to improve symptoms in AF patients who remain symptomatic on adequate rate control therapy.*
2) *all trials that have compared rhythm control and rate control to rate control alone have resulted in neutral outcomes*
3) efficacy of antiarrhythmic drugs to maintain sinus rhythm is modest;
4) safety rather than efficacy considerations should primarily guide the choice of antiarrhythmic drug especially in elderly patients
5) cathether ablation of atrial fibrillation should be considered without discrimination by age group