Rate and Rhythm Control of Atrial Fibrillation

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춘계 심혈관 통합학술대회

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Treatment of AF

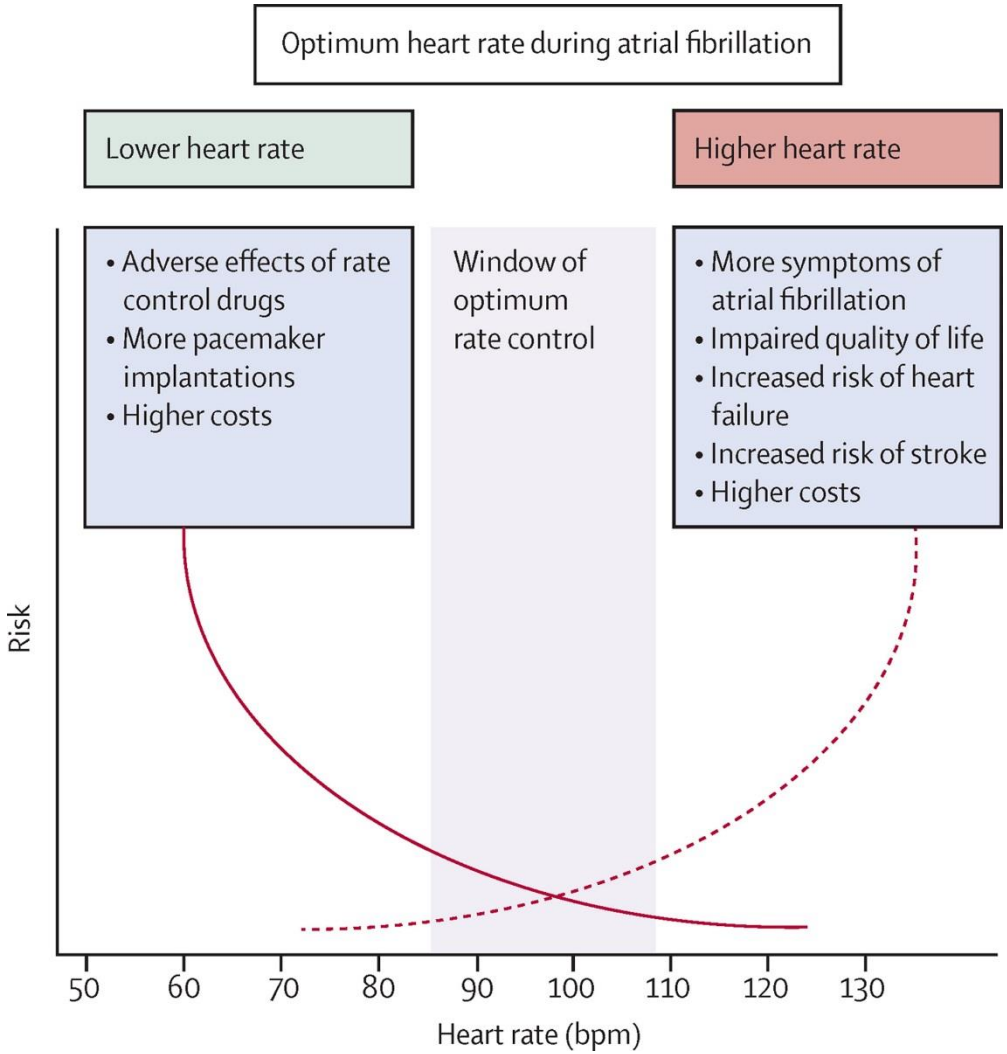
Goal

- Reducing symptoms
- Preventing complication

Strategy

- Rate control
- Rhythm control
- Stroke prevention

Rate Control



Van Gelder et al. Lancet. 2016;388:818-28.

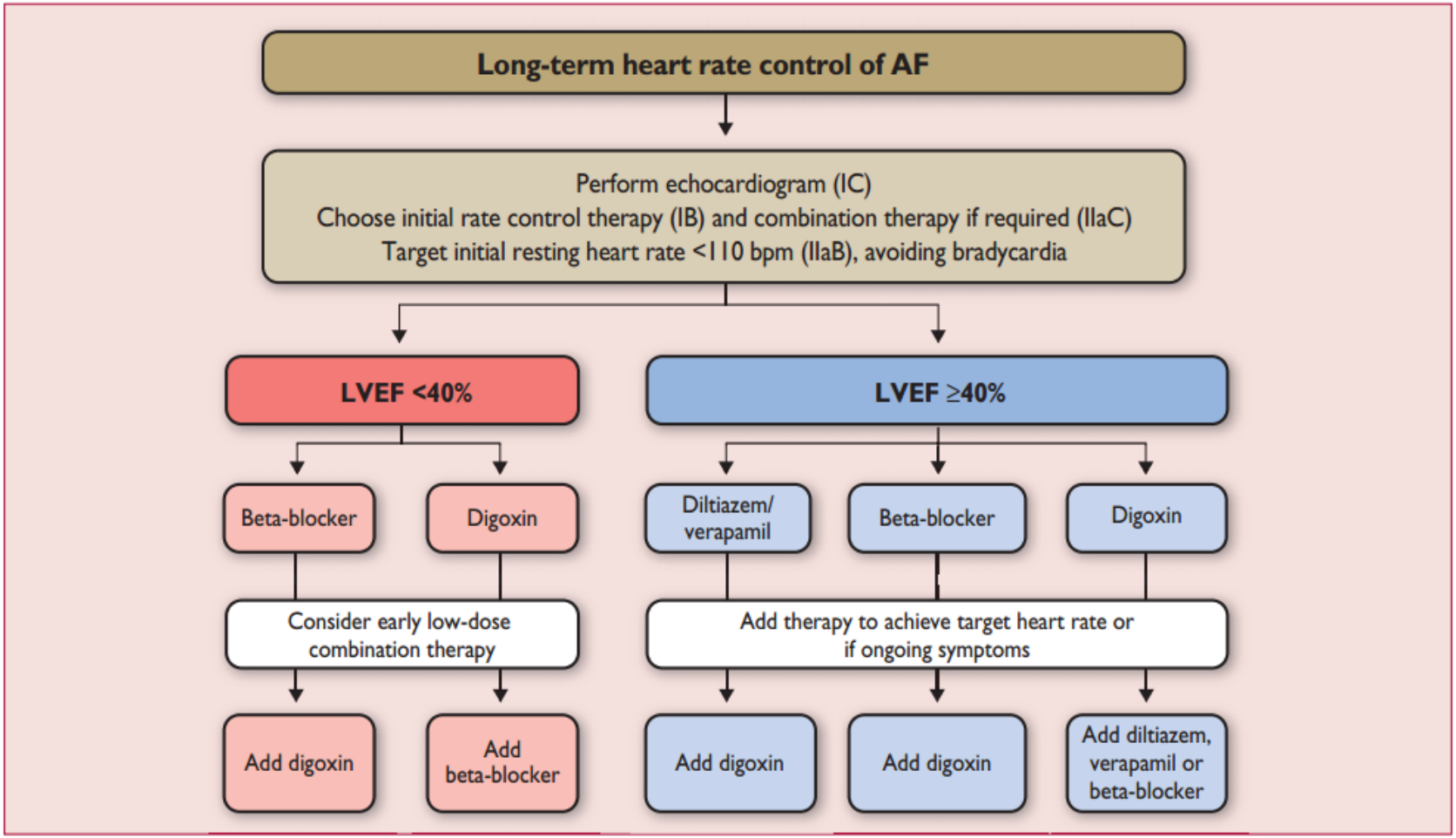
Rate Control

- **Loss of atrial kick, tachycardia and irregularity ➔ reduce ventricular filling and stroke volume**
- **Background treatment for nearly all patients**
- **A lenient rate control**
  - **Initial approach**
  - **Resting HR<110/min**
  - **Easy, safe, and effective**

Rate Control

- Beta-blockers (propranolol, bisoprolol, atenolol..)
- Non-DHP CCB (diltiazem, verapamil)
- Digoxin
  - Not effective during exercise
  - Conflicting data on cardiovascular outcomes
  - Still useful in patients with HF
- Amiodarone
  - Critically ill patients and those with HF in whom BB and digoxin are insufficient

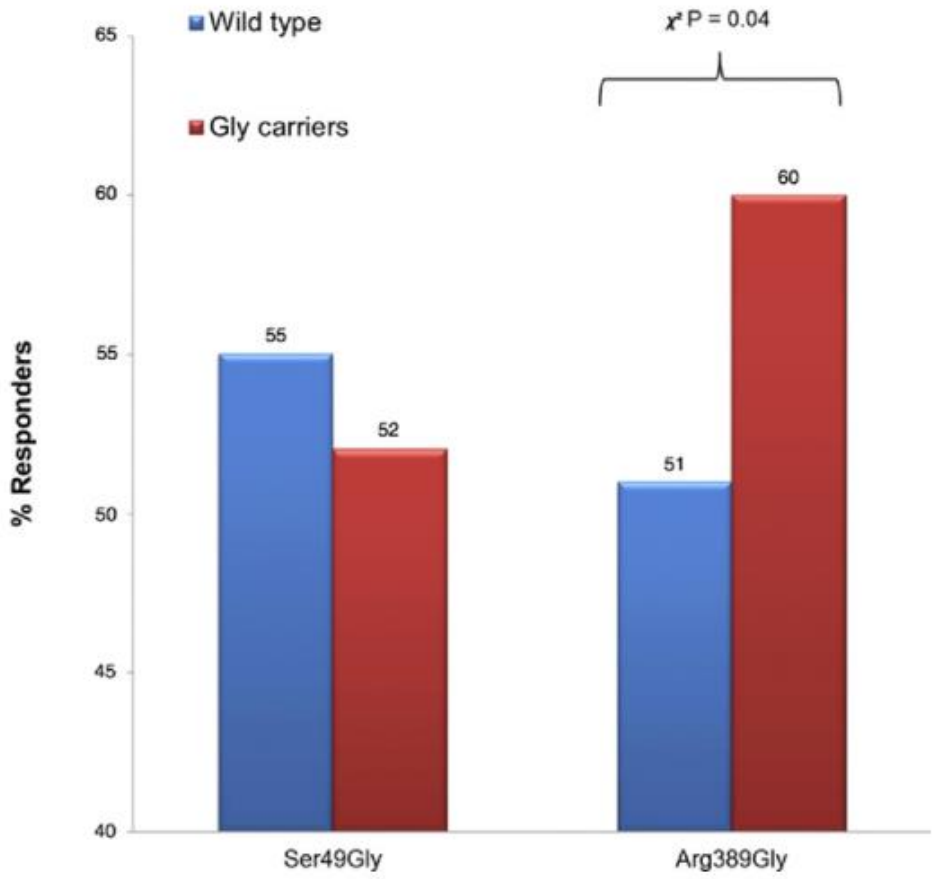
Rate Control



2016 ESC Guidelines

Genetic polymorphism and rate control

Response to Rate-Control Therapy Based on β1-AR Genotype

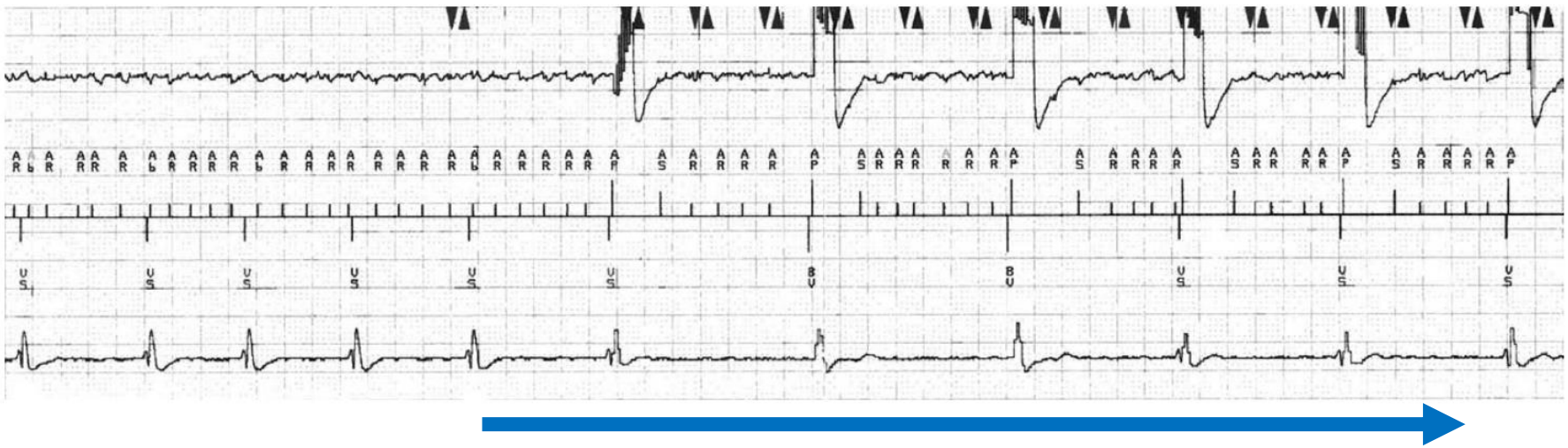


Parvez et al. J Am Coll Cardiol 2012; 59: 49–56.

Rate control by AVN stimulation

- AVNS via a RA lead positioned in the Rt. posteroseptal region.
- AVNS software uploaded to a CRT-D and can be performed automatically.
- AVNS probably reduces inappropriate shocks.

AVNS activated



Ventricular rate becomes slower

Bianchi et al. Circ Arrhythm Electrophysiol. 2015;8:562-568.

Rhythm Control

- Antiarrhythmic drugs (AAD)
- Electrical cardioversion
- Catheter ablation

Principles of AAD Therapy

- Treatment is motivated by attempts to reduce AF-related symptoms.
- Efficacy of AAD to maintain sinus rhythm is modest.
- Clinically successful AAD therapy may reduce rather than eliminate recurrence of AF.
- Drug-induced proarrhythmia or extra-cardiac side effects are frequent.

2016 ESC Guidelines

Choice of Antiarrhythmic Drug

- **Safety rather than efficacy considerations should primarily guide the choice of antiarrhythmic agent**

Aim of AAD use in AF

- Pharmacological Cardioversion
- Maintenance of Sinus Rhythm in AF

Available Drugs in Korea

- **Class Ic**
  - Flecainide
  - Propafenone
  - Pilsicainide
- **Class III**
  - Amiodarone
  - Dronedarone
  - Sotalol

Recommended Drug Doses for Pharmacological Cardioversion of AF

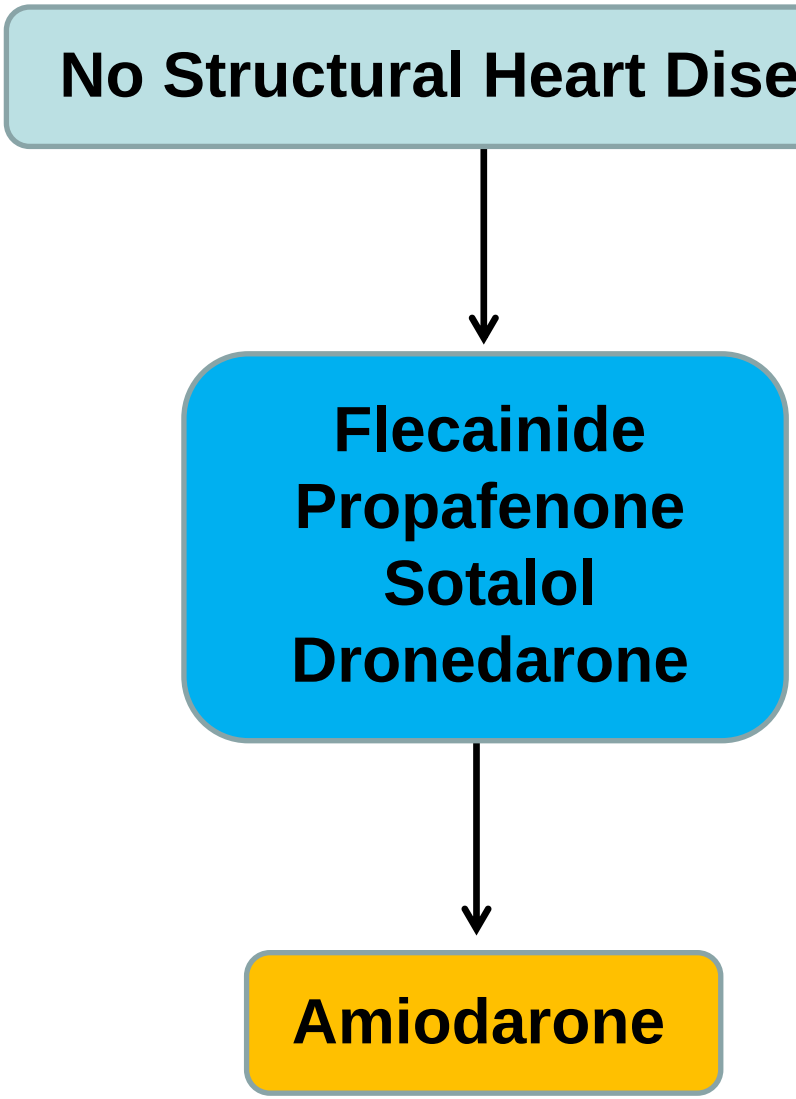
Drug	Route & Dose	Caution
Amiodarone*	Oral or IV	Hypotension, bradycardia, QT prolongation, TdP (rare) Increased INR
Flecainide	Oral, 200–300 mg X1 **Pill in the pocket**	Hypotension AFL with 1:1 AV conduction Proarrhythmia in pt with CAD or significant SHD
Propafenone	Oral, 450–600 mg X1	The same as above

*IV: 600–800 mg daily in divided doses to a total load of up to 10 g, then 200 mg QD as maintenance Oral; 150 mg over 10 min, then 1 mg/min for 6 h, then 0.5 mg/min for 18 h or change to oral dosing

Dosage and Safety Considerations for Maintenance of Sinus Rhythm in AF

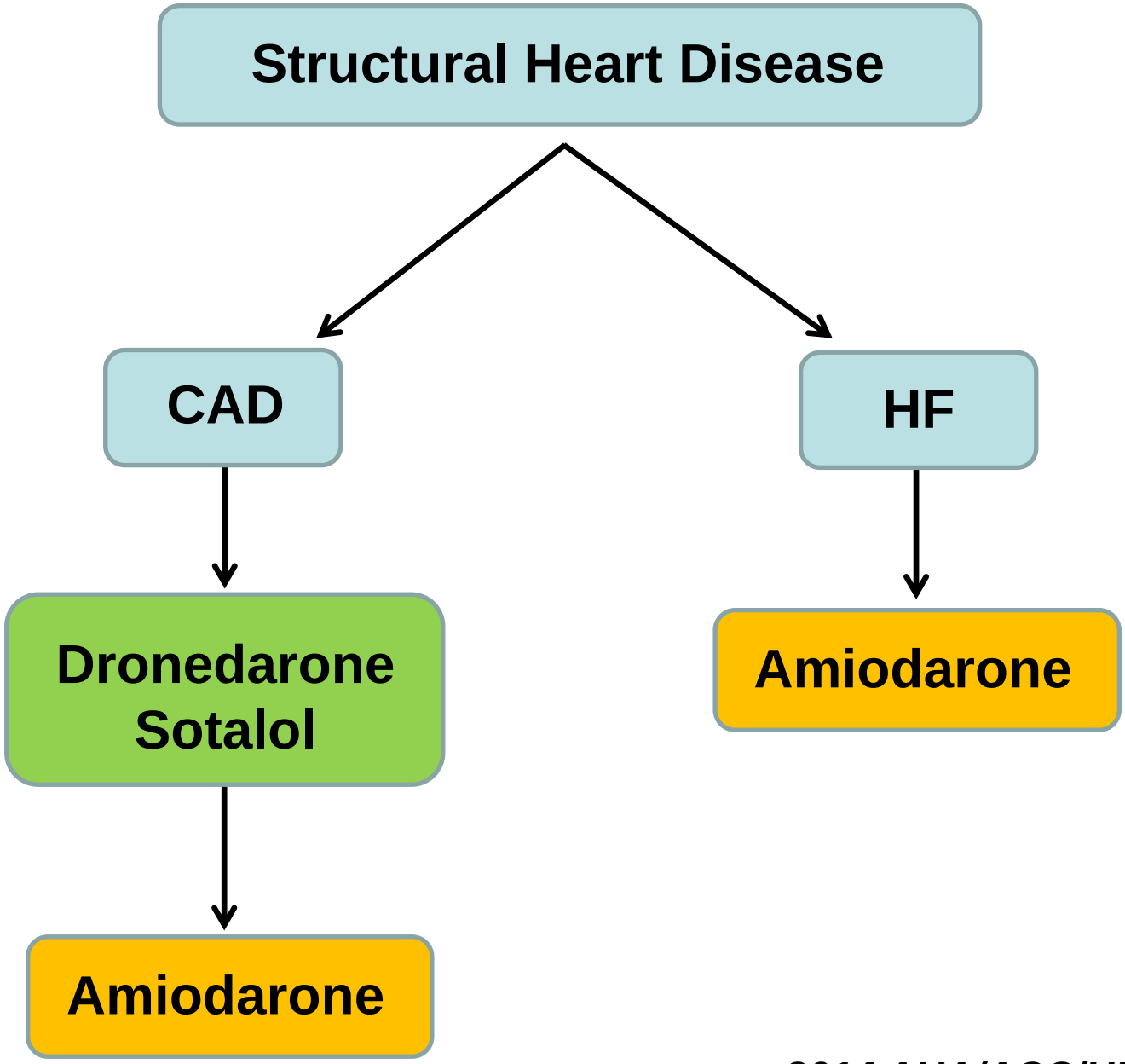
Drug	Route & Dose	Caution
Flecainide	50–200 mg bid	Sinus or AV node dysfunction HF, CAD, Atrial flutter Infranodal conduction disease Brugada syndrome Renal or liver disease
Propafenone	150–300 mg qid or 225–425 mg bid (SR)	The same as above Liver disease Asthma
Amiodarone	Oral or IV Maintenance: 100-200 mg qd	Sinus or AV node dysfunction QT prolongation, TdP (rare, Increased INR, Lung disease
Dronedarone	400 mg bid	Bradycardia, HF, LPeAF Liver disease Prolonged QT interval
Sotalol	40–160 mg bid	Prolonged QT interval Sinus or AV nodal dysfunction HF, Asthma

What to Choose?



- **Flecainide & Propafenone**
  - Not recommended with severe LVH (wall thickness >1.5 cm).
  - Should be combined with AV nodal blocking agents.
- **Sotalol**
  - with caution in patients at risk for torsades de pointes

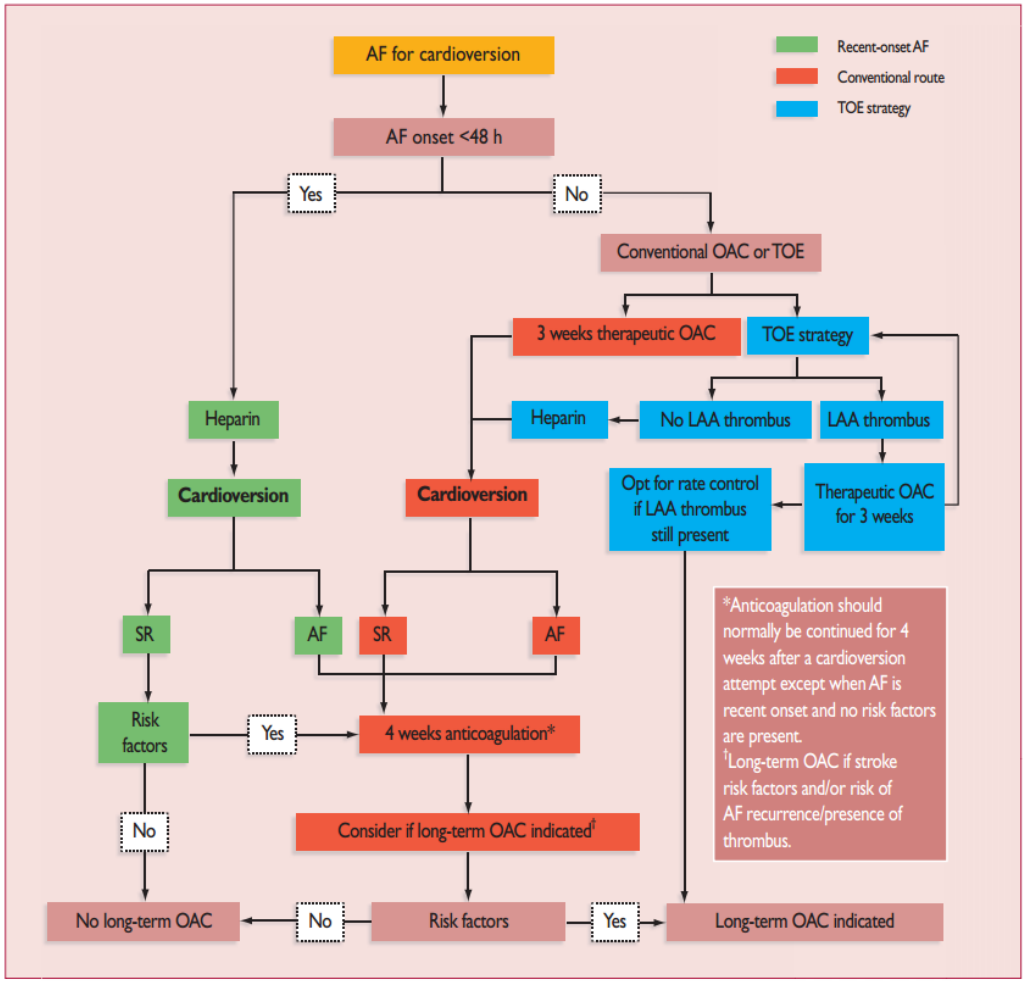
2014 AHA/ACC/HRS Guideline



2014 AHA/ACC/HRS Guideline

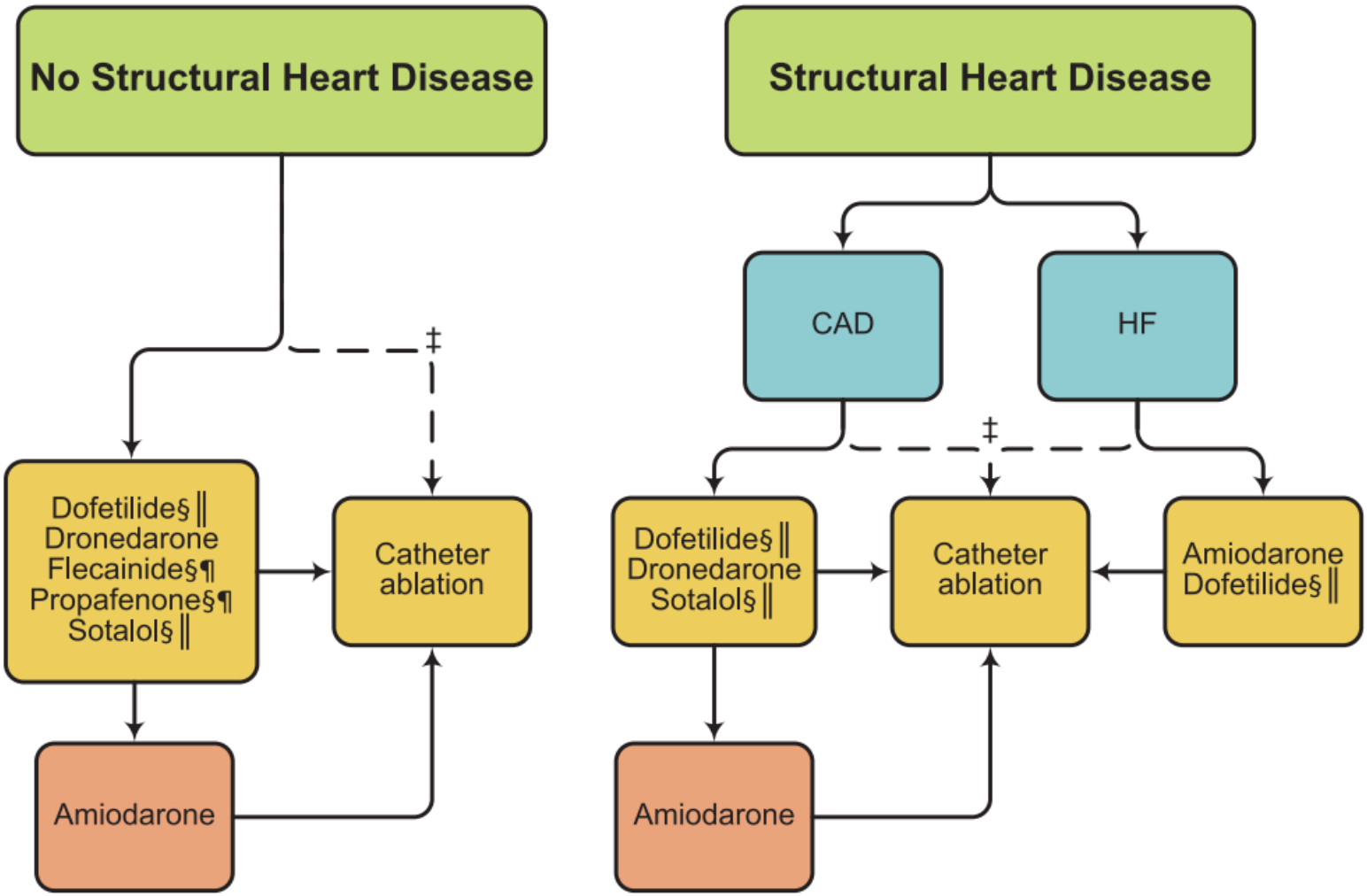
Electrical Cardioversion

- **Useful to determine if sinus rhythm is important to improve Sx**



2010 ESC Guidelines

Rhythm Control



2014 AHA/ACC/HRS Guideline

Rate vs. Rhythm Control

- **Is there anyone ever who volunteered to be in atrial fibrillation?**

Potential Benefits of Rhythm Control

- Mortality
- Stroke
- Improvements in LV function
- AF symptoms
- Exercise tolerance
- Quality of life

Well established

Rate vs. Rhythm Control Trials

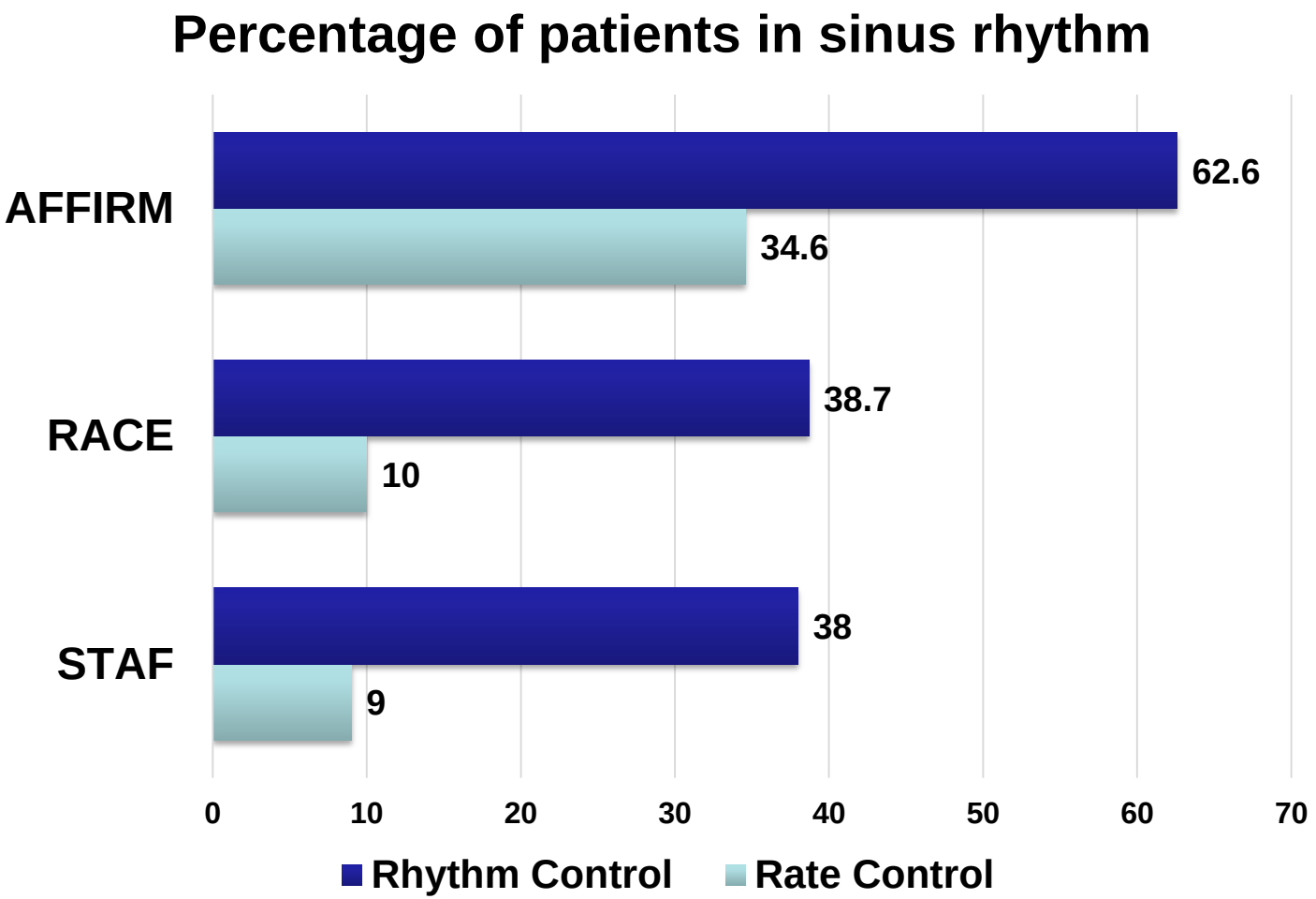
Trial	Patients (*n*)	Mean age (years)	Mean length of follow-up (years)	Inclusion criteria	Primary endpoint	Patients reaching primary endpoint (*n*)		
						Rate control	Rhythm control	*P*
PIAF[8]	252	61.0	1.0	Persistent AF (7–360 days)	Symptomatic improvement	76/125 (60.8%)	70/127 (55.1%)	0.32
AFFIRM[6]	4060	69.7	3.5	Paroxysmal AF or persistent AF, age 65 years or older, or risk of stroke or death	All-cause mortality	310/2027 (25.9%)	356/2033 (26.7%)	0.08
RACE[7]	522	68.0	2.3	Persistent AF or flutter for <1 year and 1 to 2 cardioversions >2 years and oral anticoagulation	Composite: cardiovascular death, CHF, severe bleeding, PM implantation, thromboembolic events, severe adverse effects of antiarrhythmic drugs	44/256 (17.2%)	60/266 (22.6%)	0.11
STAF[9]	200	66.0	1.6	Persistent AF (>4 weeks and <2years), left atrial 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 CAFÉ[10]	205	60.8	1.7	First clinically overt persistent AF (≥7 and <2 years), 50–75-year old	Composite: death, thromboembolic events; intracranial/ major haemorrhage	1/101 (1.0%)	4/104 (3.9%)	>0.71
AF-CHF[11]	1376	66	3.1	LVEF≤35%, symptoms of CHF, history of AF (≥6 h or ECV <last 6 months)	Cardiovascular death	175/1376 (25%)	182/1376 (27%)	0.59

Europace 2011;13:1517–1525.

Why?

- **Rhythm intervention: AAD or cardioversion**
- **Rate control was compared with frequently inadequate rhythm control**
- **Survival benefits of sinus rhythm were offset by the risks of drug therapy.**
- **The severity of the atrial substrate for AF**

Pitfalls in Rate vs. Rhythm Control Trials



Verma A, Natale A. Circulation. 2005;112:1214-1231.

AFFIRM On-Treatment Analysis

Covariates Significantly Associated With Survival

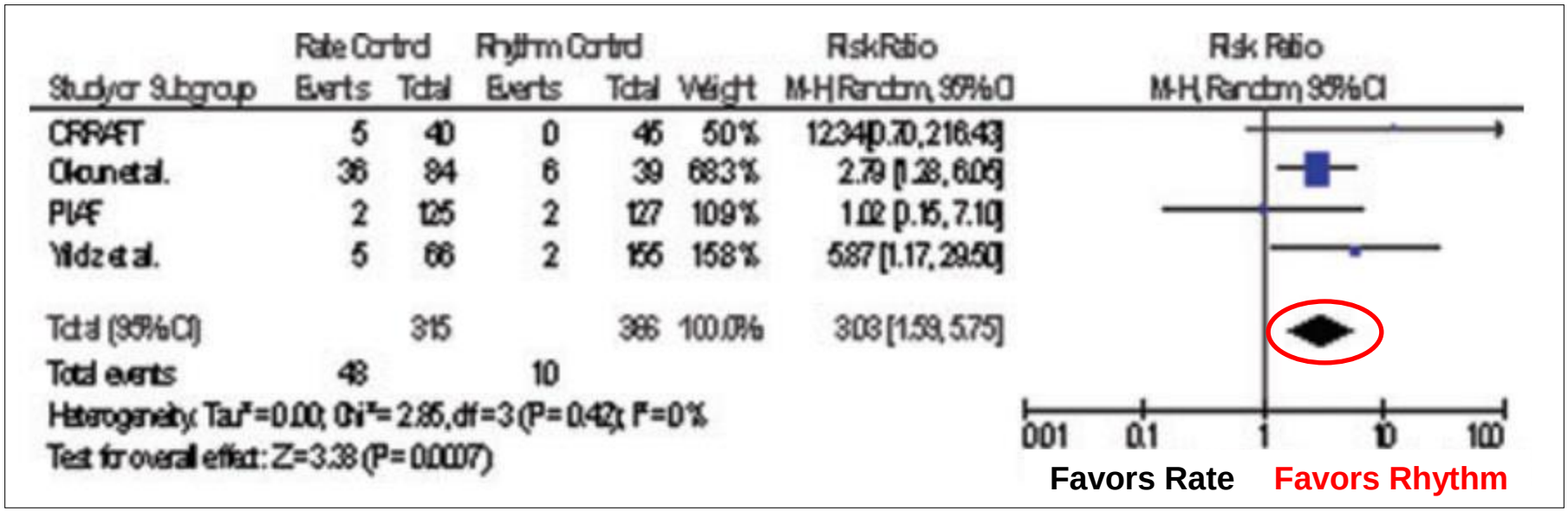
Covariate	P	HR	HR: 99% CI	
			Lower	Upper
Age at enrollment*	<0.0001	1.06	1.04	1.08
Coronary artery disease	<0.0001	1.65	1.31	2.07
Congestive heart failure	<0.0001	1.83	1.45	2.32
Diabetes	<0.0001	1.56	1.22	2.00
Stroke or TIA	<0.0001	1.54	1.17	2.05
Smoking	<0.0001	1.75	1.29	2.39
First episode of AF	0.0067	1.27	1.01	1.58
Sinus rhythm	<0.0001	0.54	0.42	0.70
Warfarin use	<0.0001	0.47	0.36	0.61
Digoxin use	<0.0001	1.50	1.18	1.89
Rhythm-control drug use	0.0005	1.41	1.10	1.83

* per year of age

AFFIRM Investigators. Circulation. 2004;109:1509-1513

Rate vs. Rhythm Control

All cause mortality in AF patients younger than 65



PACE 2013; 36:122–133

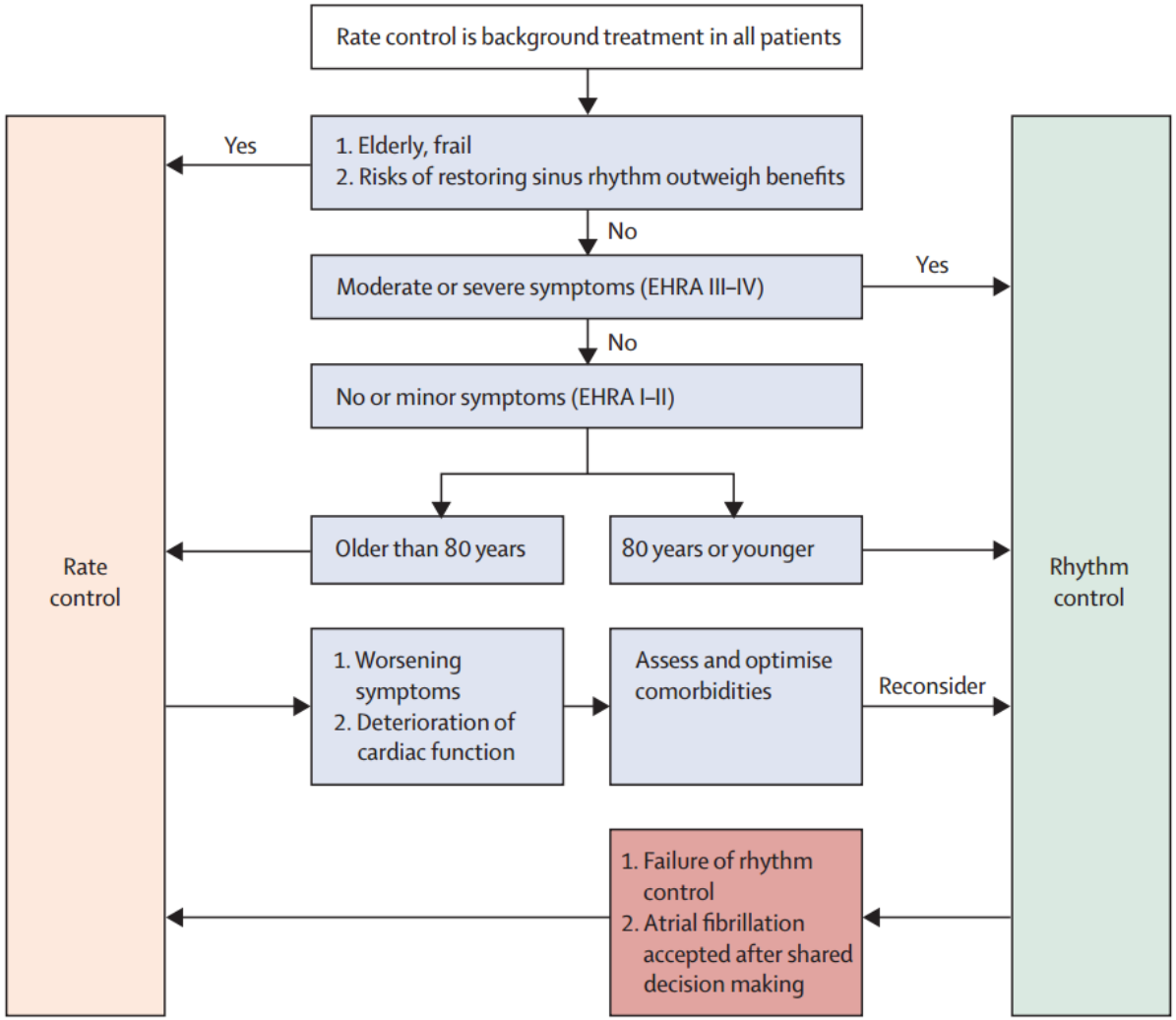
Rhythm vs. Rate Control

- **Rhythm control**
  - Persistent symptoms despite rate controls
  - Difficulty in achieving adequate rate control
  - Tachycardia-mediated cardiomyopathy
  - Young age (<65 years)
  - Patient preference

Vs.

- **Rate control**
  - Long history of AF
  - Older age
  - Untreated underlying cause
  - Enlarged LA (>55 mm)

Treatment Strategy



Van Gelder et al. Lancet. 2016;388:818-28.

Young Patient without Symptom

- **Pro**
  - May prevent stroke, HF, increased mortality
  - May become symptomatic later on
  - Easier at an early stage in younger patients with PAF
  - Ablation is superior to AAD

- **Con**
  - AF by itself has not been shown to increase mortality
  - Stroke risk is independent of rhythm control strategies
  - AADs for many years with risk of side effects
  - Complications and recurrences of ablation

EHJ 2014;35:1439–1447.

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Thank You.

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