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SPECIAL EDITION

FOOD & ARRHYTHMIAS



Post-Operative Atrial Fibrillation Is Best Treated With Rate Control

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Background

- Post-Operative Atrial Fibrillation (POAF) is the most common complication of cardiac surgery (incidence: 30÷50%).

Camm A.J. et al, European Heart Journal 2010, 31:2369–2429

- Major concerns about management of POAF include:
 - Adequate prophylaxis
 - Rate control
 - Sinus rhythm restoration
 - Thrombo-embolism prevention

Echahidi N. et al, Journal of the American College of Cardiology 2008, 51:793–801

Background

- Previous trials have evaluated effects of rate control strategy versus sinus rhythm restoration in the treatment of atrial fibrillation:
 - **AFFIRM trial (4060 pts, follow-up at 5 yrs)**
 - Primary endpoint (overall mortality): rhythm-control strategy offers no survival advantage over the rate-control strategy
 - Secondary endpoints: there are potential advantages, such as a lower risk of adverse drug effects, with the rate-control strategy

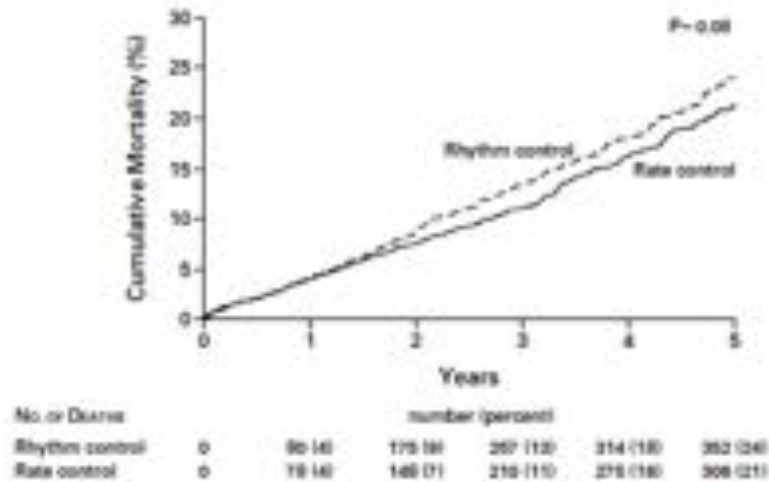


TABLE 4. ADDITIONAL ADVERSE EVENTS OR CLINICAL FINDINGS PROMPTING DISCONTINUATION OF A DRUG.*

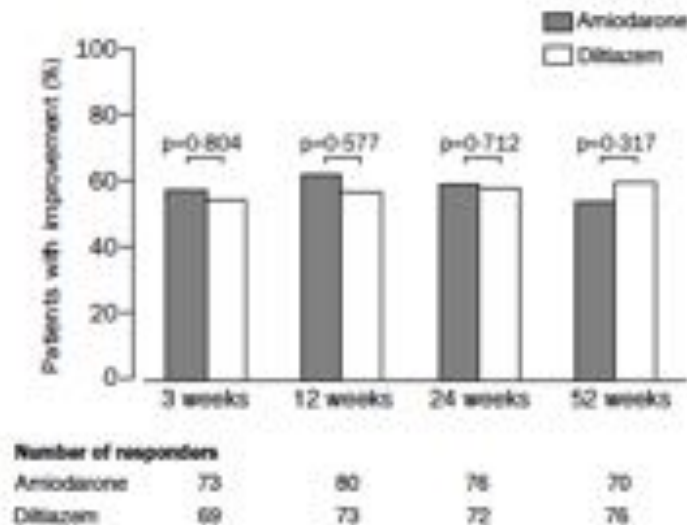
Event	Overall (N=4060)	Rate- Control Group (N=2031)	Rhythm- Control Group (N=2029)	P Value†
	no. of patients (%)			
Congestive heart failure	79 (2.4)	37 (2.1)	42 (2.7)	0.58
Pulmonary event	132 (4.6)	24 (1.7)	108 (7.8)	<0.001
Gastrointestinal event	162 (5.0)	35 (2.1)	127 (8.0)	<0.001
Bradycardia	169 (5.1)	64 (4.2)	105 (6.0)	0.001
Prolongation of the corrected QT interval (>528 msec)	35 (1.1)	4 (0.3)	31 (1.9)	<0.001
Other	590 (19.8)	176 (14.0)	414 (25.4)	<0.001

AFFIRM investigators, New England Journal of Medicine 2002, 347:1825-33

Background

- **PIAF trial (252 pts with recent onset of AF, follow-up at 1 yr)**

- Primary endpoint (improvement in symptoms): the therapeutic strategies of rate versus rhythm control yielded similar clinical results overall.



Hohnloser S.H. et al, Lancet 2000, 356: 1789-94

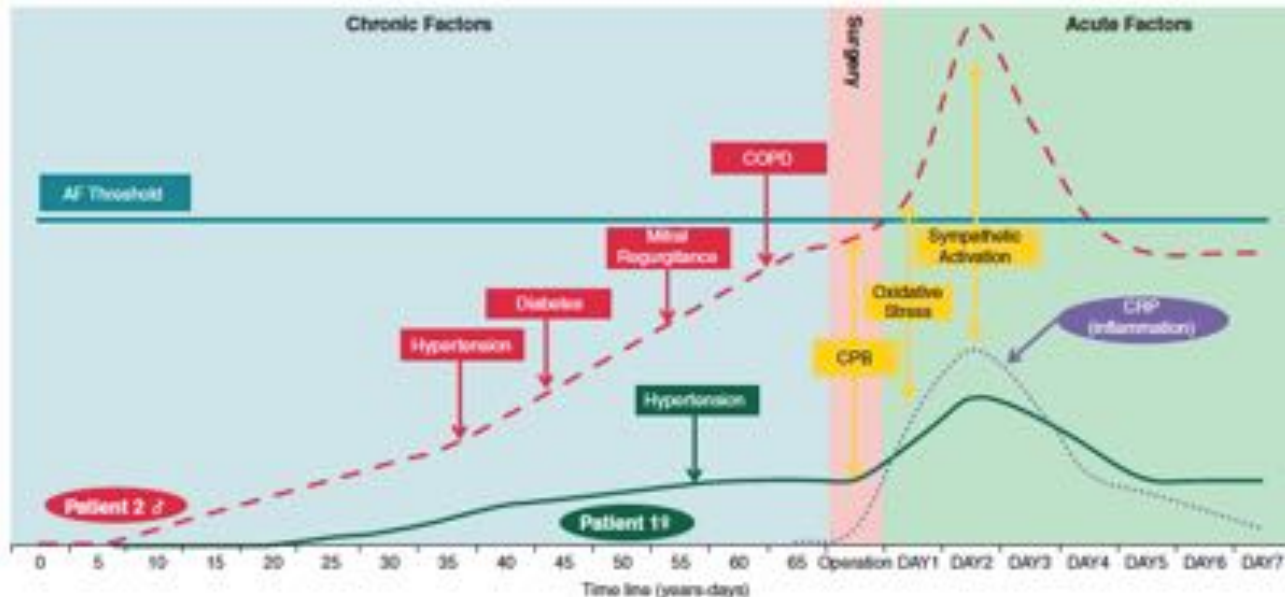
- **RACE trial (352 pts with persistent AF, mean follow-up: 2.3 yrs)**

- Primary endpoint (quality of life, QoL): No significant changes in QoL could be demonstrated between the two treatment groups

Hagens V.E. et al, Journal of American College of Cardiology 2004, 43:241–7

Background

- POAF pathophysiology involves several mechanisms and is related with acute factors depending on cardiac surgery.

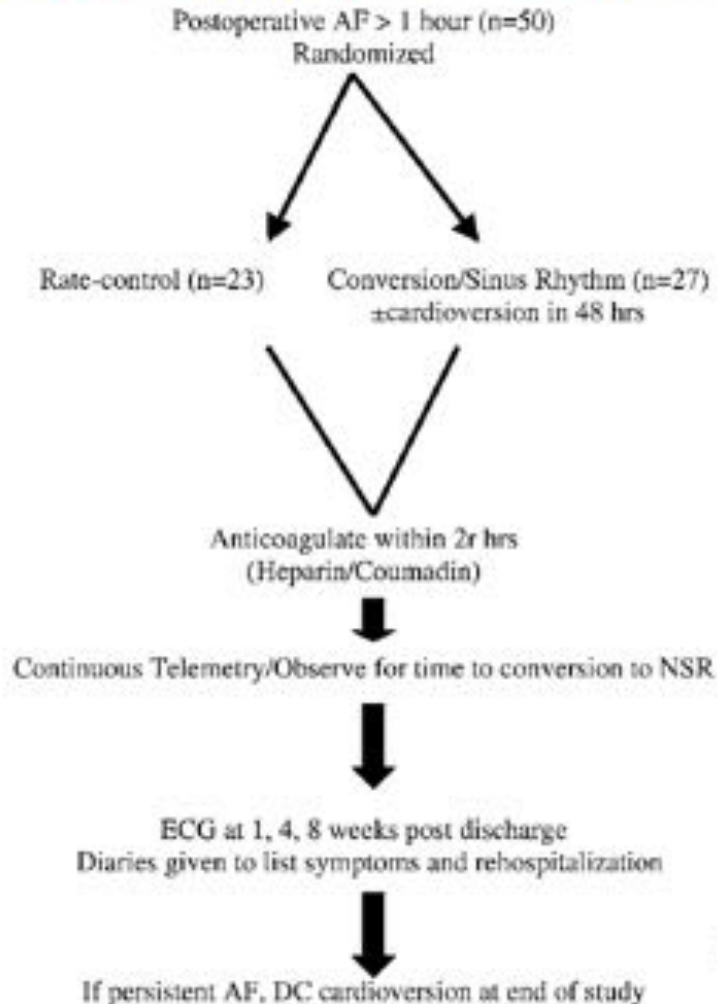


Maesen B. et al, Europace 2012, 14:159–174

- POAF is often a self-limited condition that does not need an aggressive antiarrhythmic treatment if hemodynamics is stable.

Rate control vs. Rhythm control

Rate-Control Versus Conversion Strategy in Postoperative Atrial Fibrillation: Trial Design and Pilot Study Results



*John K. Lee, George J. Klein, Andrew D. Krahn,
Raymond Yee, Kelly Zarnke, Christopher Simpson
and Allan Skanes*

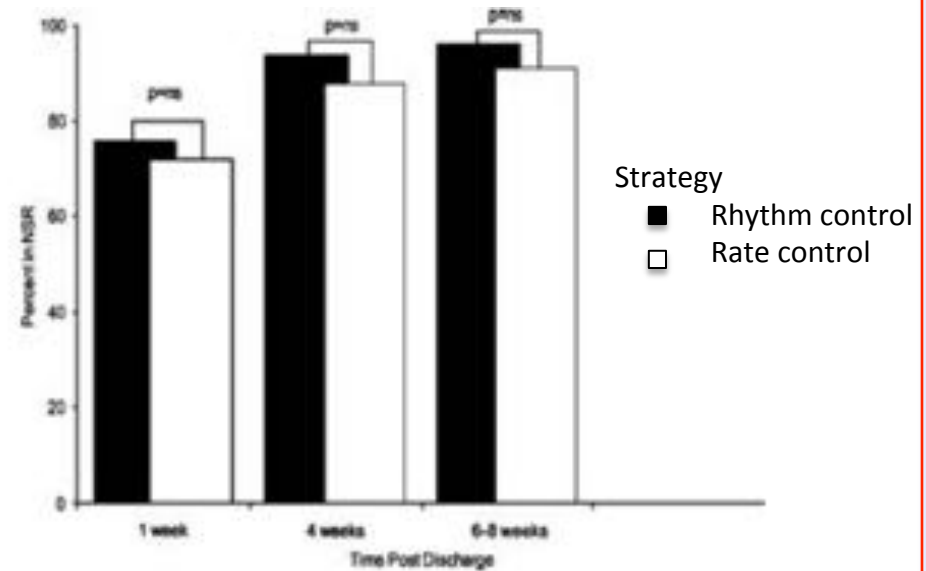
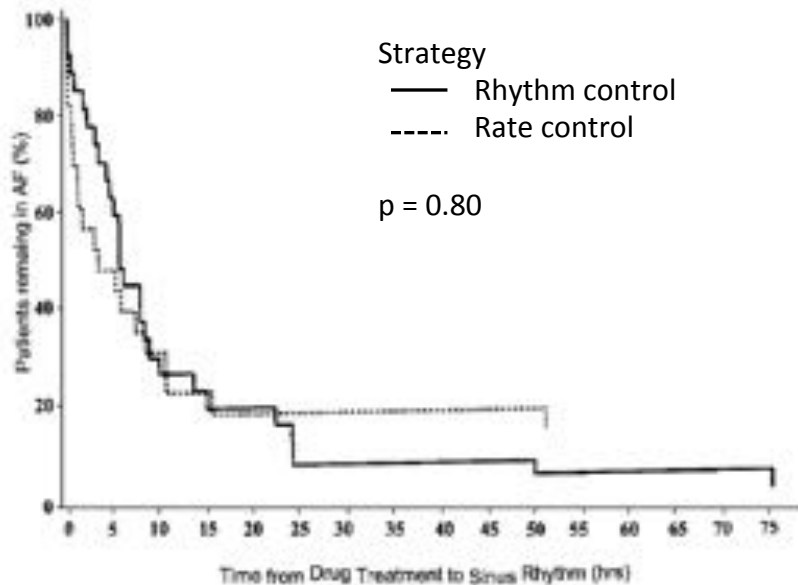
*The Arrhythmia Service, University of Western Ontario, London
Health Sciences Centre, Ontario, Canada*

Characteristic	Conversion* (n = 27)	Rate control (n = 23)
Age	67 ± 7	70 ± 5
Sex (% male)	78	78
LVEF (%)	49 ± 1	47 ± 11
Preoperative beta-blockers (%)	63	61
Valvular surgery (%)	30	30
Smoker (%)	67	56
Ventricular response at randomization	131 ± 35	123 ± 32
Diabetes (%)	19	23
Occurrence of AF (postoperative day)	3 ± 1	3 ± 1
Bypass-pump time (min)	91 ± 29	84 ± 21
Chronic obstructive pulmonary disease	15	13
Hypertension (%)	48	52
Preoperative calcium-channel Blockers (%)	63	38



Rate control vs. Rhythm control

Results



Conclusions: ***“Feasibility of rate-control as an alternative to aggressive attempts at preserving sinus rhythm in patients with POAF”***

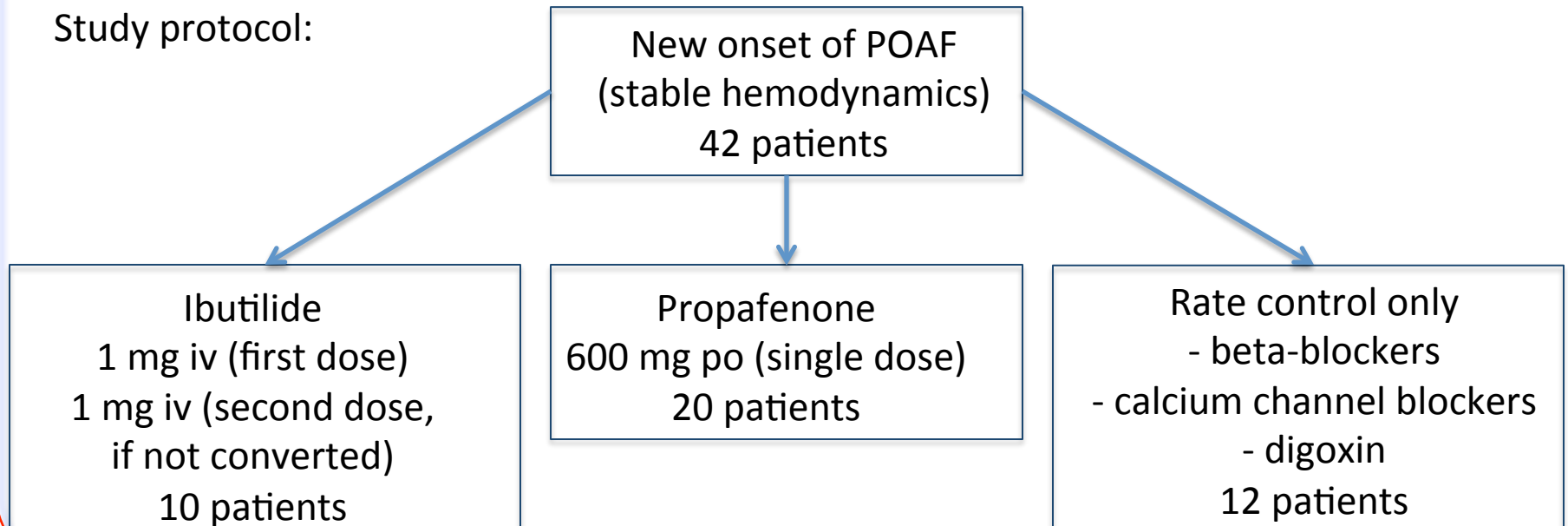
Rate control vs. Rhythm control

Propafenone versus Ibutilide for Post operative Atrial Fibrillation following cardiac surgery: neither strategy improves outcomes compared to rate control alone (The PIPAF study)

Richard Soucier¹, David Silverman², Melecio Abordo³,
Preet Jaagosild⁴, Ademola Abiose⁵, KP Madhusoodanan⁶,
Michael Therrien¹, Neal Lippman¹, Honora Dalamagas¹, Ellison Berns¹

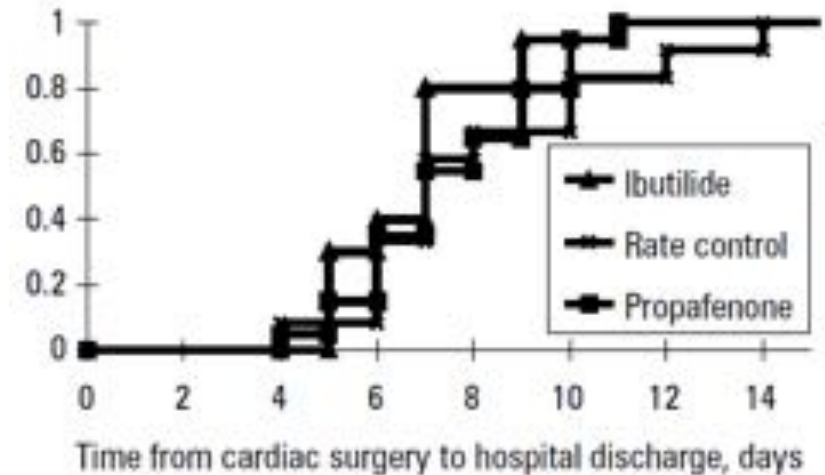
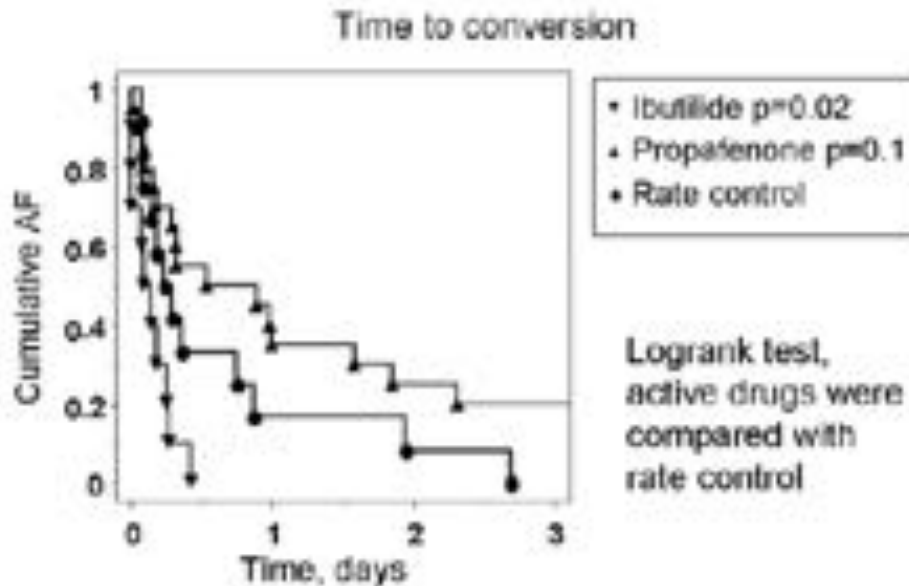
Med Sci Monit, 2003; 9(3): PI19-23

Study protocol:



Rate control vs. Rhythm control

Results



Conclusions

- ***“Most patients will eventually convert to and remain in sinus rhythm regardless of treatment strategy”.***
- ***“Decreased hospital length of stay does not appear to be associated with early conversion of POAF”.***

Drugs

Rate-control

Table 2 Dosage, Advantages, and Side Effects of Drugs Used for Rate Control in POAF

Drugs	Adult Dosage	Advantages	Side Effects
Digoxin	0.25–1.0 mg IV then 0.125–0.5 mg/day IV/PO	Can be used in heart failure	Nausea, AVB moderate effect in POAF
Beta-blocker drugs			
Esmolol	500 µg/kg over 1 min then 0.05–0.2 mg/kg/min	Short-acting effect and short duration	Might worsen congestive heart failure; can cause bronchospasm, hypotension, AVB
Atenolol	1–5 mg IV over 5 min repeat after 10 min then 50–500 mg b.i.d. PO	Rapid onset of rate control (IV)	
Metoprolol	1–5 mg IV over 2 min then 50–500 mg b.i.d. PO	Rapid onset of rate control (IV)	
Calcium channel blocker drugs			
Verapamil	2.5–30 mg IV over 2 min then 80–120 mg/day b.i.d. PO	Short-acting effect	Might worsen congestive heart failure, AVB
Diltiazem	0.25 mg/kg IV over 2 min then 5–15 mg/h IV		

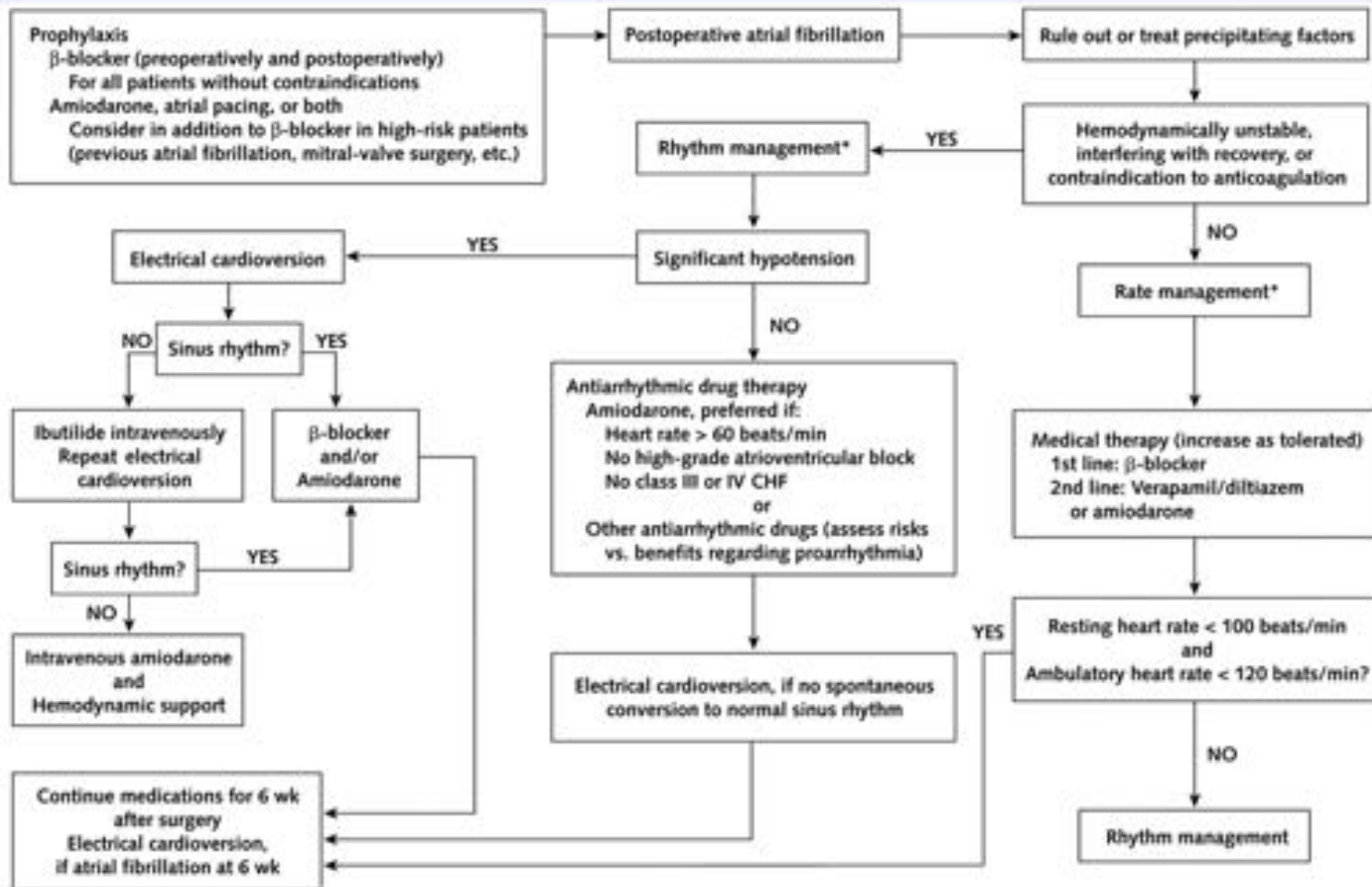
Rhythm-control

Table 3 Dosage, Advantages, and Side Effects of Drugs Used for Rhythm Control in POAF

Drugs	Adult Dosage	Advantages	Side Effects
Amiodarone	2.5–5 mg/kg IV over 20 min then 15 mg/kg or 1.2 g over 24 h	Can be used in patients with severe LV dysfunction	Thyroid and hepatic dysfunction, torsades de pointes, pulmonary fibrosis, photosensitivity, bradycardia
Procainamide	10–15 mg/kg IV up to 50 mg/min	Therapeutic levels quickly achieved	Hypotension, fever, accumulates in renal failure, can worsen heart failure, requires drug level monitoring
Ibitulide	1 mg IV over 10 min, can repeat after 10 min if no effect	Easy to use	Torsades de pointes more frequent than amiodarone and procainamide

Echahidi N. et al, Journal of the American College of Cardiology 2008, 51:793–801

Example of Flow-chart



*Anticoagulate if no contraindication. Warfarin is preferred for high-risk patients (age ≥ 65 y, CHF, diabetes mellitus, hypertension, or stroke or TIA). Aspirin, 325 mg, may be an acceptable alternative in low-risk patients. May consider heparin until INR is therapeutic, if history of stroke or TIA.

ESC/EACTS Guidelines

Recommendations for post-operative AF

Recommendations	Class ^a	Level ^b	Ref. ^c
Oral β -blockers are recommended to prevent post-operative AF for patients undergoing cardiac surgery in the absence of contraindications.	I	A	186, 187
If used, β -blockers (or other oral antiarrhythmic drugs for AF management) are recommended to be continued until the day of surgery.	I	B	187, 196
Ventricular rate control is recommended in patients with AF without haemodynamic instability.	I	B	196
Restoration of sinus rhythm by DCC is recommended in patients who develop post-operative AF and are haemodynamically unstable.	I	C	

Pre-operative administration of amiodarone should be considered as prophylactic therapy for patients at high risk for post-operative AF.	IIa	A	186–188
Unless contraindicated, antithrombotic/anticoagulation medication for post-operative AF should be considered when the duration of AF is ≥ 48 h.	IIa	A	195
If sinus rhythm is restored successfully, duration of anticoagulation should be for a minimum of 4 weeks but more prolonged in the presence of stroke risk factors.	IIa	B	195
Antiarrhythmic medications should be considered for recurrent or refractory postoperative AF in an attempt to maintain sinus rhythm.	IIa	C	
Sotalol may be considered for prevention of AF after cardiac surgery, but is associated with risk of proarrhythmia.	IIIb	A	186

Conlusions

- POAF is a common but often self-limited complication of cardiac surgery.
- Trials conducted so far have demonstrated that, in hemodynamically stable patients, rhythm control does not improve clinical outcomes compared to rate control alone.
- The drugs used to rate control have fewer side and arrhythmogenic effects than those required for the restoration of sinus rhythm.
- Further studies with larger cohorts of patients are needed to clarify the best treatment of POAF, as those already performed for non-surgical related atrial fibrillation.