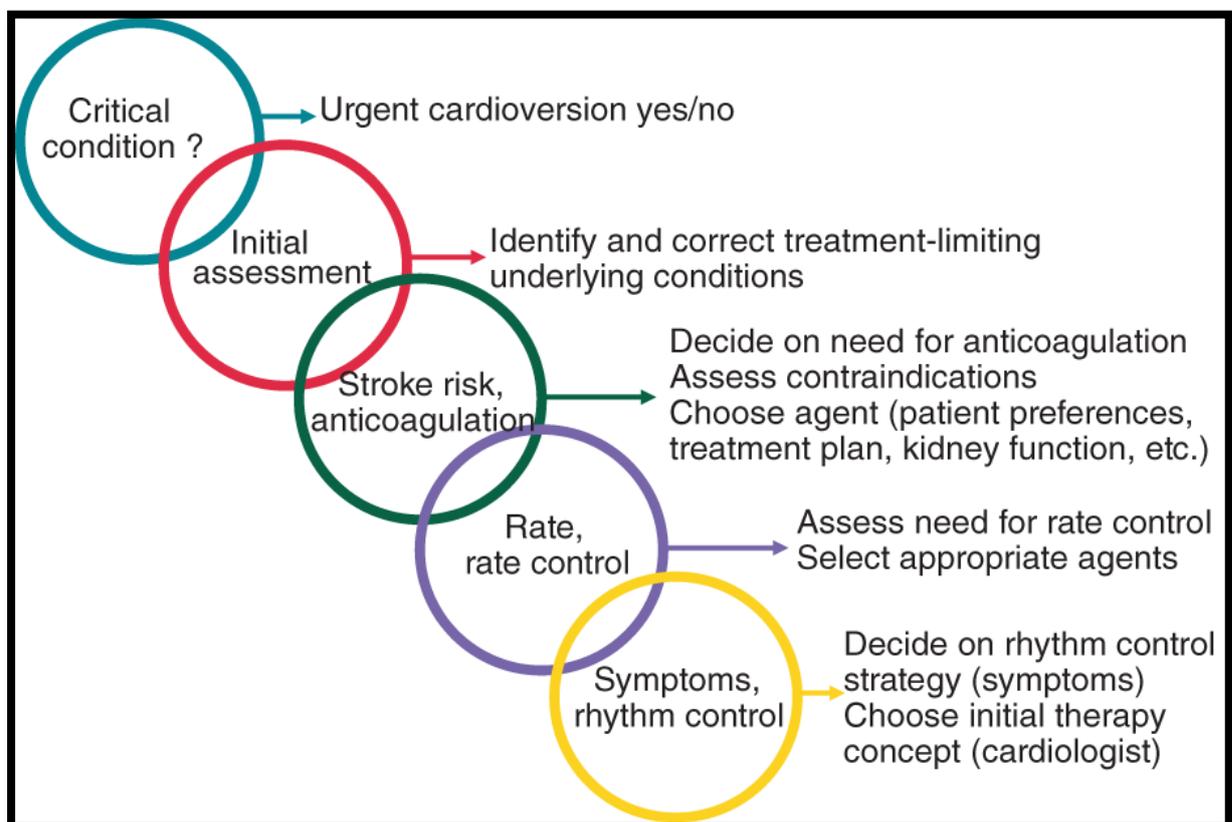


## Rate vs Rhythm Control in Atrial Fibrillation – A never-ending conundrum?

### Introduction

Atrial fibrillation (AF) is a common condition affecting an estimated number of 33.5 million adults globally (1). It is independently linked with a 1.5 to 2-fold increase in mortality (2,3) and associated with increased morbidity due to stroke and congestive cardiac failure (4,5).

Many patients with AF are asymptomatic, obtaining their diagnosis as an incidental finding during opportunistic screening or investigation for other diseases. Management of the condition involves a multi-disciplinary team approach – often including general practitioners, nurse specialists, cardiologist, general physicians, etc. The fourth AFNET/EHRA consensus report (6) proposed a stepwise approach to decision making in these patients (Figure 1).



**Figure 1:** Stepwise approach to decision making in patients with AF. Adapted from the report on the 4th AFNET/EHRA consensus conference (6).

### Rate control in chronic AF

This is an integral part of management and is often sufficient to control AF-related symptoms. Pharmacological rate control options include beta-blockers, rate-limiting calcium channel blockers and digoxin, or combination therapy. Beta-blockers and rate-limiting calcium channel blockers are the preferred first-line agents because of their rapid onset of

action and increased effectiveness at high sympathetic tones compared to digoxin (7,8). These agents are generally well tolerated and may already be taken by the patient for a separate indication. Calcium channel blockers should be avoided in patients with reduced ejection fraction (EF) due to their negative inotropic effects (9,10). A target resting heart rate (HR) of <110bpm seems appropriate as data from the RACE 2 trial found no difference between strict rate control (resting HR <80bpm and HR during moderate exercise <110bpm) or lenient rate control (resting HR <110bpm) (11).

In patients where pharmacological rate control fails, an invasive 'pace-and-ablate' strategy may be considered. It involves ablation of the atrioventricular (AV) node and implantation of a VVI pacemaker to control the ventricular rate. This is often a last resort as the procedure is non-reversible and patients are rendered pacemaker-dependent for the rest of their lives.

### Rhythm control in chronic AF

A rhythm control strategy is often the treatment of choice in symptomatic patients where the restoration of sinus rhythm is desirable. The ESC 2016 guideline suggests that it should also be considered as the preferred management in pre-excited AF and AF in pregnancy (Class IIa, Level of Evidence C) (12). In addition, it should be considered in patients with adult congenital heart disease (eg. Fontan repair) due to their risk of rapid decompensation.

The options for rhythm control are electrical or pharmacological cardioversion. Electrical cardioversion restores sinus rhythm quicker, is more effective and is associated with shorter hospitalisation duration (13–15). Conversely, pharmacological cardioversion does not require sedation or fasting. Pharmacological options include propafenone, flecainide, dronedarone, sotalol and amiodarone.

A recent study demonstrated an increased risk of stroke in non-anticoagulated AF patients who undergo direct current cardioversion (DCCV) (16), which is significantly reduced by anticoagulation (17). Importantly, the absence of thrombus pre-cardioversion does not negate the possibility of a stroke as it has been shown that restoration of sinus rhythm results in a fall of blood flow velocity in the left atrial appendage that may predispose to thrombus formation subsequently (18). As a result, the European (12) and American (19) guidelines both recommend pre-treatment with anticoagulation for >3 weeks or TOE-guided cardioversion in patients with an onset of AF over 48 hours, for both electrical and pharmacological cardioversion.

### Rate versus rhythm control in chronic AF

The long-term choice between a rate or rhythm control approach is complex and involves the consideration of numerous factors. There have been various studies in the past two decades

that have compared a rate versus rhythm control strategy – some pivotal randomised trials are shown in Table 1.

Current evidence does not suggest a difference in outcome between rate or rhythm control in chronic AF (20–25). However, it should be noted that an increase in hospitalisation and reported side effects were observed with medications used for rhythm control. As a result, many physicians tend to opt for a rate control strategy initially but would consider an anti-arrhythmic strategy if the former fails to provide adequate HR or symptom control.

### Catheter ablation

Catheter ablation (CA) has emerged as a treatment for AF with increasing level of evidence to support its use. It is achieved through pulmonary vein isolation using radiofrequency or cryo-ablation. It has been shown to be effective in restoring SR in patients with AF and heart failure and has the ability to improve LV function, functional capacity and HF symptoms when compared to a rate control strategy (26,27). The AATAC study also demonstrated that CA is superior to amiodarone in achieving freedom from AF at long-term follow-up in patients with persistent AF, implantable cardioverter-defibrillator (ICD) in situ, NYHA II or III, and left ventricular EF<40% (28). Most recently, further evidence has emerged on the effectiveness of CA. The authors of CASTLE-AF were able to demonstrate a reduction in composite of death from any cause or hospitalisation for worsening heart failure in 363 patients with symptomatic AF, NYHA class II-IV, left ventricular EF<35% and an ICD in situ using CA compared to medical therapy (rate or rhythm control) (29).

### Conclusion

Rate versus rhythm control in chronic AF has been a matter of debate over the past two decades with no real difference observed between either approach. However, recent evidence suggests that perhaps the discussion should now focus on medical therapy versus catheter ablation and that we as physicians should strongly consider catheter ablation as a possible therapeutic option for our patients with chronic AF.

**Table 1:** Trials comparing rate and rhythm control in AF

<b>Study</b>	<b>Participants</b>	<b>Rate control agent used/permitted</b>	<b>Rhythm control agent used/permitted</b>	<b>Mean follow-up</b>	<b>Findings from primary endpoint</b>
<b><i>PIAF trial, 2000</i></b> (25)	n=252	Diltiazem	Amiodarone	12 months	No difference in patient reported symptoms
<b><i>AFFIRM trial, 2002</i></b> (24)	n=4060	Beta-blockers, CCB (verapamil or diltiazem), digoxin or combination therapy	Amiodarone, disopyramide, flecainide, moricizine, procainamide, propafenone, quinidine, sotalol, dofetilide or combination therapy	3.5 years	No difference in survival outcomes
<b><i>Van Gelder et al, 2002</i></b> (23)	n=522, persistent AF after previous DCCV	Beta-blockers, CCB (verapamil or diltiazem), digoxin or combination therapy	DCCV followed by flecainide, propafenone or amiodarone	2.3 years	No difference in composite endpoint of CVS death, heart failure, thromboembolic complications, bleeding, PPM implantation and severe adverse effects of drugs
<b><i>STAF trial, 2003</i></b> (22)	n=200, persistent AF	Beta-blockers, CCB (verapamil or diltiazem), digoxin or AV node ablation/modification ( $\pm$ PPM implantation)	External or internal cardioversion followed by class I anti-arrhythmic agents, sotalol or amiodarone	19.6 months	No difference in the composite endpoint of death, CPR, cerebrovascular event, and systemic embolism
<b><i>Roy et al, 2008</i></b> (21)	n=1376, AF and heart	Beta-blockers with digoxin or AV node ablation with PPM	Amiodarone, sotalol or dofetilide with DCCV within 6	37 months	No difference in time to death from cardiovascular causes

	failure (EF <35%)	implantation	weeks and 3 months if SR is not achieved		
<b>Gillinov et al, 2016</b> (20)	n=523 with new-onset AF after cardiac surgery	Not specified	Amiodarone with DCCV if AF persisted for 24-48 hours	60 days	No difference in the total number of days of hospitalisation

CCB = calcium channel blockers, CVS = cardiovascular, PPM = permanent pacemaker, CPR = cardiopulmonary resuscitation, SR = sinus rhythm

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