



# What is New for Treatment of Atrial Fibrillation

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## Rate control acceptable alternative for treatment of atrial fibrillation

Despite a wide range of inclusion criteria, atrial fibrillation (AF) and patient characteristics and primary and secondary study end points, the randomized trials showed a remarkably consistent outcome: rate control is at least as effective as rhythm control in preventing morbidity and mortality. In AFFIRM, there was even a statistical trend towards superiority of rate control over rhythm control. Thus, rate control is adequate for most patients with persistent AF

However, what is meant by “adequate” rate control? Currently, the RACE investigators are conducting a prospective randomized trial, RAte Control Efficacy in permanent AF (RACE II) to evaluate a lenient versus a rigid rate control approach for patients with permanent AF to tackle this issue.

## Which patient benefits from rhythm control?

To answer this question it is necessary to look back to the patient groups studied. The typical patient treated in the trials was a 70 year old male with complaints of fatigue, dyspnea and palpitations from recurrent AF with a history of hypertension. Indeed, for this patient, rate control strategy is an attractive option. However, several subgroups can be identified likely to gain from restoration of sinus rhythm. Clinical determinants influencing the benefit of either rate or rhythm control are the type of AF, severity of AF related complaints and underlying diseases. Especially in (severe) symptomatic patients, patients presenting with a first episode of AF and in patients without stroke risk factors (i.e. those in whom oral anticoagulation may be discontinued) rhythm control is still first choice.

## Rhythm control – how?

Anti-arrhythmic drugs remain first choice therapy. Class I, II or III antiarrhythmic drugs are equally effective except for amiodarone that is superior but yet only moderately successful. However, a season ticket approach, including 1-2 cardioversions per year may be a very attractive option for many patients.

In order to improve success rate of rhythm control antiarrhythmic drugs should be initiated before cardioversion. Adding calcium channel blockers to class I or III antiarrhythmic drugs also may further improve outcome. New data suggest that institution of

angiotensin receptor blockers or angiotensin converting enzyme inhibitors may contain additional beneficial effects on outcome. Whether new antiarrhythmic drugs eventually may enhance efficacy as compared to amiodarone remains to be awaited.

In severely symptomatic patients non-pharmacological treatment strategies are promising, especially transvenous pulmonary vein isolation with use of radio frequency energy. Success rates up to 80% have been demonstrated although in 30-50% of the patients a second procedure is needed and antiarrhythmic drugs frequently should be continued

## Anticoagulation, for rate and rhythm control

A very important issue highlighted by RACE and AFFIRM is that rhythm control therapy does not prevent stroke. It was observed from RACE that 21 of the 35 thromboembolic complications occurred under rhythm control, mostly at an INR below the therapeutic range of 2-3. Six patients had the event after cessation of oral anticoagulant therapy, with 5 of them in sinus rhythm. The majority (23 out of 25) of strokes occurred while receiving inadequate anticoagulation therapy. One reason for this was that in the rhythm control group it was allowed to stop oral anticoagulation if sinus rhythm was present for >1 month after cardioversion. This may have caused the excess strokes in this treatment arm in RACE since thrombosis risk probably persists despite sinus rhythm. Moreover, the list of accepted stroke risk factors in AF of higher age (above 65 years), hypertension, diabetes, atrial enlargement, left ventricular dysfunction and a previous thromboembolic event, does not contain heart rhythm. Also emboli originating in the thoracic aorta and the carotid artery may contribute to stroke in patients with AF. So, with restoration of sinus rhythm in patients with AF, other stroke risk factors remain present. Furthermore, an important RACE finding is that interruption of oral anticoagulation itself, with fluctuating INR levels, is an identifier of increased risk of thromboembolic events and bleeding. Therefore, one of the main lessons learned from the randomized studies is that anticoagulation must be continued if stroke risk factors are present even if patients maintain sinus rhythm. So, also patients with paroxysmal AF need adequate anticoagulation if they have stroke risk factors. So, oral anticoagulation is indicated in every patient with persistent atrial fibrillation with risk factors for thromboembolic complications, irrespective of the heart rhythm.