

Atrial Fibrillation

Cardiac rate control or rhythm control could be the key to AF therapy

Recent studies have proven that an option of pharmacologic and non-pharmacologic therapy is available to patients who suffer from AF.

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Atrial fibrillation (AF) is the most common cardiac arrhythmia in the general population with an overall incidence of 1%.¹ In those over 65, the prevalence of AF is 6% to 10%.^{1,2} AF appears to be an independent risk factor for mortality, with AF patients demonstrating an almost twofold increase in mortality after controlling for confounding variables.³ This observation accounts for the change in the way physicians have approached AF in the past decade. The conventional wisdom shifted from “atrial fibrillation is a benign rhythm disturbance seen frequently with aging” to “sinus rhythm at all costs for everyone.” Evidence to support this latter strategy had, however, yet to be presented.

What are the symptoms and risk factors?

In AF, most symptoms, but not all, are caused by a rapid and irregular ventricular rate. AF may result in decreased exercise tolerance, fatigue, and cardiovascular symptom-related factors, such as palpitations, presyncope, and

dyspnea. AF is also an important risk factor for stroke. Potential advantages of sinus rhythm include the possibility of fewer symptoms, better exercise tolerance, a lower risk of stroke, eventual discontinuation of long-term anticoagulant therapy, better quality of life, and longer survival. Several of the aforementioned advantages of sinus rhythm are subjective end points and not easy to quantify in clinical trials. The end point of mortality, being a ‘hard’ end point, was recently evaluated in several trials including Atrial Fibrillation Followup Investigation of Rhythm Management (AFFIRM), Rate Control versus Electrical Cardioversion (RACE), and Pharmacological Intervention in Atrial Fibrillation (PIAF).^{4,5,6,7}

What do recent studies have to say?

AFFIRM was designed to determine whether restoration and maintenance of sinus rhythm is associated with a lower all-cause mortality

when compared to the alternative strategy of rate control in patients with AF. Between 1995 and 1999, AFFIRM followed 4,060 patients for a mean of 3.5 ± 2.5 years; AFFIRM has been the largest study of atrial fibrillation ever undertaken, and all the subjects in this study had at least one other risk factor for stroke or death. The mean age of the patients was 69.7 ± 9.0 years, where 70.8% had hypertension and 38.2% had coronary artery disease. Of the 3,311 patients who had echocardiograms, 64.7% had left atrial enlargement and left ventricular function was depressed in 26%.

Subjects who were randomized to the rhythm control strategy received one or more of several different antiarrhythmic drugs, including amiodarone and sotalol. In the rate control strategy, digoxin, beta blockers, and/or calcium channel blockers were allowed; anticoagulation was encouraged in both treatment arms. When clinically indicated, patients could also be crossed over to the alternate rate or rhythm control strategy.

Mortality at five years was 23.8% in the rhythm control and 21.3% in the rate control groups ($p=0.08$). More patients in the rhythm-control group were hospitalized than in the rate control group and there were more adverse drug effects in the rhythm control group. In both groups, the majority of strokes occurred after warfarin had been stopped or when the international normalized ratio (INR) was subtherapeutic. Rhythm control offered no significant benefit

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with respect to exercise tolerance or quality of life.

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Frequently Asked Questions:

Atrial Fibrillation: Rate versus rhythm control

Questions:

Answers:

Which drugs are useful in the maintenance of sinus rhythm?

Several antiarrhythmic medications are useful in the maintenance of sinus rhythm including:

- Propafenone
- Flecainide
- Sotalol
- Amiodarone

What are the 'non-pharmacologic' treatments?

- In the rate control arm, one may consider AV node ablation to prevent the rapid ventricular response to AF.
- Sophisticated pacemaker pacing algorithms can be used to prevent or to terminate AF, thus reducing 'AF burden'.
- Other options in the rhythm control arm include ablation techniques to terminate AF. These can be catheter based, such as pulmonary vein isolation, or surgical such as radiofrequency (RF) or microwave ablation during open-heart surgery.

What are the benefits/risks of maintaining sinus rhythm?

The theoretical benefits of maintaining sinus rhythm are:

- improved quality of life
- reducing the risk of thromboembolism
- preventing atrial remodelling thus reducing the risk of recurrence of atrial fibrillation
- preventing tachycardia induced cardiomyopathy thus possibly reducing mortality

The risks of maintaining sinus rhythm are:

- adverse drug effects, in particular:
- proarrhythmia, including Torsades de Pointes
- organ toxicity, especially with amiodarone
- increased ventricular rates during Afib/flutter, especially with drugs with class Ia and Ic properties
- symptomatic adverse effects, eg. GI, CNS toxicity
- the risk of thromboembolism surrounding conversion and during followup

How do we interpret the results?

While the AFFIRM study results may seem to indicate an advantage to the rate control strategy, the results may apply only to the type of patient who was eligible for the study and was actually enrolled (requiring both the patients and treating physician's willingness to be randomized to a rate control strategy). The results are also not applicable to the younger patient population, who have no risk factors for stroke or death. Echoing the AFFIRM results, RACE, a European study (n=522) with similar objectives, also observed a trend toward a reduced incidence of death and other adverse events in the rate-control group (17.3% vs. 22.6%). RACE was a prospective randomized study of patients with recurrent, persistent AF. The central hypothesis was that rate control is not an inferior strategy compared to rhythm control. The pre-specified criterion for non-inferiority was a difference of 10% or less in the primary end point, a result that was achieved in the trial.

It may be inferred from the results of the previous two studies that attempting to restore and maintain sinus rhythm is deleterious for patients. It is more informative, however, to interpret the results in the context of the specific patient popu-

lations studied. The patients studied were elderly with at least one concomitant risk factor for stroke, and patients with recurrent persistent AF. In addition, they were presumably not so severely symptomatic that sinus rhythm restoration was thought to be absolutely necessary. Among these populations the strategy of rate control yields lower overall mortality, fewer strokes, and

In patients over 65, the prevalence of AF is 6% to 10%”

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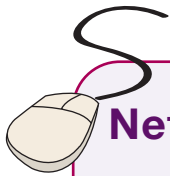
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fewer hospitalizations. For these patients, it may be advisable to pursue rate control as the preferred management strategy.

What kind of treatment and prevention are available?


Although quality of life is a difficult parameter to measure, there have been studies evaluating this in AF patients.^{8,9,10} The CTAF⁸ (Canadian Trial of Atrial Fibrillation) study evaluated the impact of symptomatic AF and its treatment on health-related quality of life. A symptom checklist (SF-36) and AF severity scale (AFSS) were filled out at baseline, three months, and twelve months. The investigators found that quality of life improves with treatment regardless of the drug used for treatment. This effect was found to be larger in patients in whom the treatment resulted in sustained sinus rhythm.

It would be simplistic to infer from the recent data that there should be one universal strategy for all patients with AF. In the more symptomatic patient population, often younger patients with 'lone' AF and no additional stroke

Take-home message

- AF is the most common cardiac arrhythmia in the general population.
- Symptoms are caused by rapid and irregular ventricular rate.
- Common symptoms include decreased exercise tolerance and fatigue.
- Cardiovascular symptoms include palpitations, presyncope, and dyspnea.

risk factors, rhythm control may still be the preferred management strategy. In those with even a single risk factor for stroke in addition to AF, regardless of rate or rhythm control strategy being used, anticoagulation therapy should be lifelong. In patients who do not have intractable symptoms during AF, a rate control strategy is entirely reasonable as an initial approach. A trial of rate control is particularly indicated if antiarrhythmic drugs are less than completely effective or cause even moderate adverse effects.

As for many other conditions, fully informed patients can contribute importantly to the decision-making process for this common and vexing disorder. 

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