

A Comparison of Rate Control and Rhythm Control in Patients with Atrial Fibrillation: The Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Investigations NEJM 347: 23 1825-33.

I. Background

Although the relative risks and benefits of rate vs. rhythm control are of paramount importance in day to day management of atrial fibrillation, studies addressing these issues have emerged only recently. There is a dearth of data suggesting any benefit of either rate or rhythm control on stroke, mortality and patient symptoms. Most investigations into rhythm control of atrial fibrillation have focused on the endpoint of how well a drug can maintain sinus rhythm, presuming that maintaining sinus rhythm will result in superior patient outcomes. Studies of heart rate control focus on how well the rate is controlled, again assuming that this is a surrogate for important patient outcomes. A trial addressing these issues, the largest to date, the AFFIRM study randomized 4060 outpatients from the US and Canada to a rate or rhythm control strategy.

A. Inclusion criteria (clinical judgment of investigators): atrial fibrillation likely to be recurrent, was likely to cause death, long term-treatment was warranted, no contraindications to anticoagulation, patient could undergo trial of at least two drugs, and treatment could begin right after randomization.

1. criteria seem reasonable though causing death seems to be quite a prediction
2. more than 1/3 were enrolled after their first episode; more than 90% had their qualifying episode within 6 weeks of enrollment
3. The mean age was 70 years. 71% had hypertension and 38.2 % had CAD

B. Strategies

1. Rhythm control: drug chosen by physician; choices included: amiodarone, disopyramide, flecainide, moricizine, procainamide, propafenone, quinidine, sotalol, or combos of these drugs. Guidelines were imposed (not mentioned)
2. Rate Control: beta-blockers, diltiazem or verapamil, digoxin or combinations of these drugs. Heart-rate during atrial fibrillation was assessed at rest and during activity.
3. After two attempts at rate or rhythm control failed, patients could be considered for radio-frequency ablation, a maze procedure, or pacing.

II. Are the Results of the Study Valid?

A. Was the assignment of patients to treatment groups randomized?

1. Yes. Randomized (allocation concealed) and blinded (outcome assessors and monitoring committee)

B. Were all the patients who entered the trial properly accounted for at the End of the trial?

1. 71 patients withdrew their consent and 26 patients were lost to follow up (they do not specify from which group)
2. Average 3.5 yrs follow-up (maximum 6 years).
3. Analysis was intention to treat
 - a. 248 (secondary to CHF) crossed to from rate to rhythm control and 514 (inability to maintain SR and drug effects) crossed from rhythm to rate control.

C. Were groups similar at the start of the trial?

1. Yes, there were no significant differences.

D. Aside from the experimental intervention, were the groups treated equally?

1. No. Patients in the rhythm control group who were in sinus rhythm could have their anticoagulation discontinued (as early as one month into study).
 - a. during the trial, more than 85% of patients in rate-control were on warfarin while approximately 70% of patients in rhythm control were on warfarin.

III. What are the results?

A. How large was the treatment effect?

1. Mortality in rate-control 25.9% (310) and rhythm 26.7% (356) RRI 12% (-0.9- 28)
 - a. Five years 34.6% of rate control in NSR and 62.6% in NSR in rhythm control group.
 2. Secondary endpoint: death, disabling stroke, major bleeding or cardiac arrest 32.7% vs. 32.0% P=.33.
 3. Strokes : 77 in rate (5.5%) and rhythm 80 (7.1) P=.79. Mostly In patients who were sub therapeutic or off coumadin. Concurrent A-fib In 62.
 4. Major bleeding (CNS non CNS) did not differ.
 5. Hospitalization significantly different 1220 vs. 1374 P <0.001 in favor of rate control.
 - a. torsades and bradycardic arrest > in rhythm.
 - b. Pulmonary GI, bradycardic events and prolongation of QT more common in rhythm in keeping with previous findings.
 6. Subgroup analysis demonstrated a trend toward higher mortality In rhythm control in those > 65 yrs, without CHF, and with CAD
- B. Other notes
1. in rate control, beta blockers used in at least 50% of patients.
 2. in rhythm control, over 2/3 had undergone at least one trial of amiodarone.

IV. Will the results help me in caring for my patients?

- A. Can the results help me in caring for my patients?
 1. Yes, though this population seemed to be a particularly healthy population of outpatients
 - a. Rate control is safe and is not inferior to rhythm control for minimally symptomatic patients in whom AF is likely to occur after cardioversion. This conclusion has been verified in other recent studies¹
- B. Questions/Comments that I had after reading the paper?
 1. Average follow-up 3.5 years—treatment for atrial fibrillation life long. Note decline of patients in rhythm control in NSR as trial progressed and that rhythm was assessed only on the day of evaluation (no ambulatory monitoring).
 3. Anticoagulation should be continued (even after cardioversion.—strokes occurred in those who were sub therapeutic or off.
 4. The prevalence of sinus rhythm (without any clear intervention) Seemed artificially high
 5. What about patients with low EF?
 6. Cost-effectiveness
 7. Quality of life measures.
- B. Were all important outcomes considered?
 1. Yes. Hard endpoints including mortality, stroke, and Quality of life. Maintenance of NSR was not a primary endpoint! Also, the many side-effects of antiarrhythmic therapy Became manifest.

¹ Van Gelder IC et al. A comparison of rate and rhythm control in patients with recurrent persistent atrial fibrillation (RACE). N Engl J Med. 2002;347:1834-40.

Hohnloser SH et al. Rhythm or rate control in atrial fibrillation—Pharmacological Intervention in Atrial Fibrillation (PIAF); a randomized trial. Lancet 2000;356:1789-94.