

Rate and rhythm control showed similar symptom improvement in atrial fibrillation

Hohnloser SH, Kuck KH, Lilienthal J, for the PIAF Investigators. Rhythm or rate control in atrial fibrillation—Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomised trial. *Lancet*. 2000 Nov 25;356:1789-94.

QUESTION

In patients with atrial fibrillation (AF), how do rate control and sinus rhythm control compare in improving symptoms?

DESIGN

Randomized (unclear allocation concealment*), unblinded,* controlled trial with 12-month follow-up.

SETTING

21 centers in Germany.

PATIENTS

252 patients who were 18 to 75 years of age (mean age 60 y, 73% men) and who presented with symptomatic persistent AF between 7 and 360 days in duration. Exclusion criteria included congestive heart failure, New York Heart Association class IV; unstable angina; acute myocardial infarction in the past 30 days; AF with mean rate < 50 beats/min; AF in conjunction with the Wolff-Parkinson-White syndrome; and coronary artery bypass graft or valve replacement in the past 3 months. Follow-up was 96%.

INTERVENTION

Patients were allocated to rate control ($n = 125$) or to rhythm control ($n = 127$). In

rate control, the therapeutic goal was to achieve an improvement in symptoms by controlling ventricular rate with the use of diltiazem, 90 mg, 2 to 3 times/d. In rhythm control, the aim was to prevent recurrent AF with the use of amiodarone, 600 mg/d for 3 weeks, and electrical cardioversion thereafter if sinus rhythm was not restored. Amiodarone, 200 mg/d, was given for maintenance of sinus rhythm.

MAIN OUTCOME MEASURES

Improvement in symptoms (elimination of palpitations and reduction of dyspnea and dizziness). Secondary outcomes were easy fatigability (6-minute walking test), change in mean heart rate, hospital admission, and quality of life.

MAIN RESULTS

The study had 90% power to detect a 50% to 70% difference in symptom improvement. The groups did not differ for symptom improvement: At 12 months, 56% of rate-control patients improved compared with 60% of rhythm-control patients ($P > 0.2$). Patients in the rhythm-control group achieved greater walking distance in 6 minutes than did patients in the rate-

control group ($P = 0.008$ at 12 mo). Heart rate decreased in both groups, from 88 to 81 beats/min in the rate-control group ($P = 0.001$) and from 86 to 78 beats/min in the rhythm-control group ($P = 0.002$). Fewer patients in the rate-control group than in the rhythm-control group were admitted to the hospital at least once (24% vs 69%, $P = 0.001$). 68% of admissions in rate control patients were for drug-related adverse effects; 67% of admissions in rhythm-control patients were for electrical cardioversion, and 27% were for amiodarone-related adverse effects. The groups did not differ for quality-of-life measures.

CONCLUSION

In patients with atrial fibrillation, rate control and sinus rhythm control did not differ for symptom improvement.

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*See Glossary.

COMMENTARY

It is unclear whether AF is better treated by suppression of tachycardia with diltiazem or by cardioversion and maintenance of sinus rhythm with amiodarone (1). The unblinded randomized trial by Hohnloser and colleagues confirmed conventional opinion that rhythm control provides better exercise tolerance than does rate control. This benefit came at a cost: more hospital admissions for electrical cardioversion or drug toxicity in the rhythm-control group.

Despite improved exercise tolerance in the amiodarone group, the groups did not differ for symptoms (palpitations, dyspnea, or dizziness) or quality of life. Equivalence of subjective outcomes may represent therapeutic equivalence, or it may be a result of subtle effects of the acknowledged bias of the investigators against rhythm control. Alternatively, bias might explain the findings: 5 rate-control patients had catheter-induced atrioventricular node modification to optimize rate control, and second-line management was left to the discretion of the investigators at each site rather than being explicitly included in the protocol.

The applicability of this study to practice is limited because most clinicians would not follow either of these simple strategies. Patients in whom amiodarone failed would probably be treated with repeated electrical cardioversion or other antiarrhythmic drugs, such as procainamide (2). Patients in whom alternative antiarrhythmics failed

would probably be treated with rate control or with an alternative procedure, such as ablation of the atrioventricular node and a permanent pacemaker (3). The study design also fails to reflect clinicians' use of pathophysiologic models of AF: The longer a patient is in AF, the more difficult it is to restore sinus rhythm. Most clinicians would more aggressively seek to restore sinus rhythm when the heart is apparently structurally normal than when mitral valve disease or atrial dilatation exists.

Two studies currently in progress (Atrial Fibrillation Follow-up Investigation of Rhythm Management [AFFIRM] and Rate Control vs Electrical Cardioversion [RACE]) may provide additional guidance on the relative merits of tachycardia suppression or cardioversion in sinus rhythm.

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