

Reply

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The AFFIRM Study: Approaches to Control Rate in Atrial Fibrillation

The optimal heart rate for patients with atrial fibrillation (AF) remains unclear; current guidelines are primarily based on clinical experience (1). Recent randomized studies suggest combining beta-blockers or calcium channel blockers with digoxin to achieve better rate control at rest and during exercise (2-4). However, I believe clarification of the "approach to control rate in AF" by the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) investigators (4) is justified.

A total of 2,027 patients were randomized to the rate control arm of the AFFIRM trial between 1995 and 1999. Of these, 248 crossed over to the rhythm-control group due to "uncontrolled symptoms" and 108 underwent AV nodal ablation due to failure of pharmacologic therapy. Rate-control data at rest are available in only 740 (36.5%) patients, which deteriorates further to 361 (17.8%) if data regarding heart-rate control during exercise are desired.

This relative lack of data may be explained by the fact that 1,055 (52%) patients were in sinus rhythm at the time of randomization. The proportion of those in the rate-control group who maintained sinus rhythm during follow-up is unclear. Published data for the entire trial population suggest a similar number (49%) remaining in sinus rhythm at study end.

Therefore, the majority of data on rate control of AF comes from a minority of patients randomized to a rate-control strategy. Because of the nature of data collection (only patients with AF at the time of assessment were selected for analysis), care should be taken in interpreting these results. The data predominantly represent patients with persistent and permanent AF and significantly underrepresent those with paroxysmal AF.

It is difficult to make conclusions on the control of ventricular rate during paroxysms of AF from this study, the occurrence of which greatly depends on variations of the autonomic tone (5).

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REPLY

We thank Dr. Van Gelder and colleagues and Dr. Shelton for their interest in our study (1). We agree with Dr. Van Gelder and colleagues that the optimal heart rate in atrial fibrillation (AF) during rest and exercise is unknown. Perhaps minimal effort to achieve rate control during AF is sufficient. However, absence of adequate rate control can lead to adverse consequences such as tachycardia-induced cardiomyopathy. Our Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) substudy was not designed to evaluate the mortality and morbidity of inadequate rate control; thus, we cannot comment on these end points.

Both ablation of the atrioventricular junction and pacemaker insertion were allowed "innovative" therapies in the AFFIRM study, and they may have contributed to the relatively frequent use of this approach. Furthermore, attempting to achieve more "stringent" rate control may have led to more symptomatic drug-induced bradycardia and subsequent pacemaker insertion in the AFFIRM study, compared to the more "lenient" criteria used in the RAte Control versus Electrical cardioversion (RACE) study. However, the patient population in the AFFIRM study was not directly comparable to that in RACE, and pacemaker implantation per capita in the U.S. is higher than in Europe. These factors may have influenced the differences between these two studies.

We agree that a long-term, prospective, randomized trial would be useful. We applaud Dr. Van Gelder and colleagues for pursuing answers to some of these difficult issues in the RAte Control Efficacy in permanent atrial fibrillation (RACE II) study.

Dr. Shelton concurs that the optimal approach to rate control remains primarily based on clinical experience. He notes that 248 patients in the AFFIRM study crossed over to the rhythm-control group, and 108 patients underwent ablation of the atrioventricular junction (1). Many patients (approximately one-half) in the

rate-control group were actually in sinus rhythm at any given visit, and their heart rates thus were not included in the data for that follow-up visit. Indeed, the numbers of patients reported for each follow-up visit interval were considerably less than the 2,027 randomized to the rate-control arm. However, the AFFIRM study experience was far larger than other studies reported to date.

Although Dr. Shelton is correct in stating that care should be taken in interpreting the data, it should be noted that patients with permanent AF are the most underrepresented segment of patients with AF in the AFFIRM study population.

Although the AFFIRM study was not designed to evaluate specific avenues to rate control, the approach we described is a composite of clinical experience utilized by a wide range of physicians who were involved in the study. Most patients can achieve adequate rate control during AF. As seen in routine clinical practice, unless permanent AF is present, not all patients will be in AF at every visit. Furthermore, the study was not designed specifically to evaluate patients with paroxysmal AF, permanent AF, or younger patients not at risk for stroke or death. It is not known whether the approaches described for the AFFIRM study patients will apply to other patient populations with AF. Clearly there is a need for carefully controlled, prospective, randomized, multicenter clinical trials to evaluate further the optimal approach to rate control in many different patient populations.

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