Assessment of Rhythm and Rate Control in Patients with Atrial Fibrillation

ERIC N. PRYSTOWSKY, M.D.
From the Clinical Electrophysiology Laboratory, St. Vincent Hospital, Indianapolis, Indiana, USA; and Duke University Medical Center, Durham, North Carolina, USA

Rhythm and Rate Control in Patients with AF. A recent series of randomized prospective clinical trials that compared rate control with rhythm control in patients with atrial fibrillation (AF) found no significant difference in primary outcome between the two strategies. However, these trials lacked clear criteria for defining “successful” rate or rhythm control. Various measures have been used to gauge the success of antiarrhythmic drug therapy, including time to first recurrence of AF, any AF recurrence, AF burden, and a reduction in symptoms. Determining the success of antiarrhythmic therapy can be relatively straightforward by using how patients feel during therapy as a key endpoint. Most patients are satisfied with a major reduction in symptomatic AF episodes and can live comfortably with occasional episodes of AF. For those who are bothered by even infrequent, brief AF episodes, a treatment regimen that eliminates nearly all AF recurrences is required, although often hard to achieve. Catheter ablation may be necessary to achieve a successful outcome in these patients. Suppression of AF in a patient at high risk of stroke does not, however, remove the need for concomitant warfarin therapy. The endpoints of ventricular rate control are not clear, and the recently published rhythm versus rate control trials lacked standard criteria for judging acceptable rate control. One relatively simple method is to try and achieve a 24-hour heart rate that mimics expected normal sinus rhythm. It is important to achieve good rate control to minimize symptoms and the risk of tachycardia-mediated cardiomyopathy.

Introduction

Treatment of patients with atrial fibrillation (AF) may include stroke prevention, rate control, and rhythm control, alone or in combination. Anticoagulation issues are key, but beyond the scope of this article. Until recently, rhythm control—that is, maintenance of sinus rhythm—was regarded as superior to rate control, which allows persistence of AF using drugs to slow the ventricular rate. Rhythm control was considered to have potential advantages, such as greater symptom relief and exercise capacity, a reduced risk of thromboembolism and the need for anticoagulation, and improved ventricular function and quality of life. However, results from a series of randomized prospective clinical trials that compared the clinical outcomes of a rhythm control versus a rate control approach in the treatment of AF did not support these claims. In the AF population studied, which was generally older patients with risk factors for stroke, the two treatment strategies had similar outcomes.

Despite demonstrating equivalent clinical outcomes, the trials lacked any clear criteria about what constituted “successful” rate or rhythm control. In the absence of a consensus for successful rate or rhythm criteria, how are clinicians to be guided in the treatment of their patients? This article explores the use of appropriate endpoints for “successful” rate or rhythm control in routine clinical practice.

Assessment of “Successful” Rhythm Control

Various measures have been used to gauge the success of antiarrhythmic drug therapy, including time to first recurrence of AF, any AF recurrence, AF burden, and a reduction in symptoms. AF burden is defined as the total percent of time a patient is in AF, and is determined by the number and duration of AF episodes. Time to first recurrence of AF is a common method for judging the success of antiarrhythmic drug therapy to control AF. While this may be useful for a statistical model and for the purposes of regulatory drug approval, it has less value in the clinical care of patients. For example, a patient may have a brief recurrence of AF 2 weeks after starting drug therapy, but overall have a marked reduction in AF episodes. If such a patient feels much better, one can hardly claim failure of drug therapy because of an early recurrence of AF.

Reducing AF burden plus symptoms seems to be a better measure of success. The combination is important, as a reduction of 100 long-lasting AF episodes before drug to 20 shorter, but still fairly symptomatic, episodes during drug therapy is not a clinical success. One should remember that symptoms do not always correlate with AF and that most patients have asymptomatic episodes of AF. The problem of asymptomatic AF is nicely illustrated in the following two case studies, in which asymptomatic AF was detected during routine implantable defibrillator follow-up (Fig. 1). Neither patient had a history of AF or symptoms suggestive of the condition. As Figure 1 shows, patient 1 had AF with

Dr. Prystowsky sits on the Board of Directors and has stock options with CardioNet Inc.

This manuscript was processed by a guest editor.

Address for correspondence: Eric N. Prystowsky, M.D., The Care Group, LLC, 8333 Naab Road, Suite 400, Indianapolis, IN 46260. Fax: 317-338-9259; E-mail: eprystow@thecaregroup.com

doi: 10.1111/j.1540-8167.2006.00580.x
Asymptomatic Atrial Fibrillation Detected During ICD Follow-up

Figure 1. Detection of asymptomatic AF during ICD follow-up in two patients. ICD = implantable cardioverter defibrillator.

Figure 2. Case study of a patient with atrial fibrillation who was successfully treated with first propafenone and verapamil treatment using mobile outpatient continuous monitoring. Rhythm strips were taken during the drug free period (A), initial (B), and subsequent (C) propafenone dose times.

a variable but relatively controlled ventricular rate. Patient 2 was being paced with a resultant regular rhythm and would not have been expected to have palpitations, but was not immune to other symptoms, such as fatigue. Thus, no measure of successful rhythm suppression is without limitations.

Continuous patient monitoring with mobile cardiac outpatient telemetry (MCOT) is another approach that can be used to measure the success of antiarrhythmic therapy. Figures 2 and 3 illustrate the use of MCOT in the case of a patient with AF who was successfully treated with propafenone and verapamil. For much of the time prior to drug treatment, the patient was in AF (Fig. 3). Administration of low-dose propafenone reduced the number of AF episodes, which were finally abolished when propafenone dosage was increased. Although the lower dose of propafenone substantially reduced AF burden and might have been considered a clinically acceptable endpoint, the patient remained symptomatic. Increasing the dose of propafenone resulted in absolutely no AF, and the patient felt fine.

Judging the success of antiarrhythmic therapy is not really a difficult issue and can be achieved by using common sense endpoints. For rhythm control, the key is how the patient feels during drug therapy. Unfortunately, a few patients are bothered by even infrequent brief AF episodes. For such patients, the key is to find a drug regimen that eliminates nearly all AF recurrences—a difficult task. Indeed, in these patients, catheter ablation may be needed to achieve a successful outcome. Most patients are quite satisfied with a major reduction in symptomatic AF episodes, and that is an entirely acceptable endpoint. It is important to remember, however, that suppression of AF in a patient at high risk of stroke does not obviate the need for concomitant warfarin therapy.

Assessment of “Successful” Rate Control

The lack of consensus on appropriate endpoints for judging the success of rhythm control applies equally to rate control. In fact, a striking feature of the recently published rhythm versus rate control trials was the lack of standardization in criteria for judging acceptable rate control. In the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial, rate control was defined as an average heart rate of ≤80 beats/min at rest and either a maximum of ≤110 beats/min during a 6-minute walk or an average of <100 beats/min on 24-hour Holter monitoring, with the rate not exceeding 110% of maximum predicted age-adjusted exercise rate. Compared with AFFIRM, the RAte Control versus Electrical cardioversion for persistent atrial fibrillation (RACE) trial used a rather simple definition of a resting heart rate on a 12-lead ECG of ≤100 beats/min, while HOT CAFE required a heart rate of 70–90 beats/min on a resting 12-lead ECG and ≤140 beats/min during moderate exercise.

Clearly, as these trials demonstrate, there are various ways of assessing ventricular rate control, including a resting ECG,
stress testing, or a 24-hour ECG recording. My practice is to achieve heart rate control during routine daily activities by trying to mimic what might occur if the patient had normal sinus rhythm. The assumption, though unproved, is that the optimal physiological response during sinus rhythm can be duplicated by a similar rate during AF. A 24-hour ECG recording is obtained during the patient’s usual daily activities and AV nodal blocker therapy is tailored toward achieving a mean daily rate in the range of 70–80 beats/min. Ideally, there should be few, if any, hours in which the rate exceeds 100 beats/min. Particular attention should be paid to reducing large swings in heart rate within each hour, as symptoms in AF are often related to both the overall heart rate and the variability of rate.

This technique presumes the clinician understands what a typical 24-hour sinus rate plot should be for patients in different age groups with varying cardiac function, but without AF. However, such information is not often available. Figure 4 provides some representative examples of 24-hour recordings using MCOT on three patients in normal sinus rhythm, and one from a patient with reasonably well-controlled heart rate during AF. Each point represents mean heart rate at 30-minute intervals. As the first three plots show, at times the heart rate exceeds 100 beats/min, but the mean for any particular hour is usually between 50–100 beats/min. Although not identical, all three 24-hour heart rate plots of patients in normal sinus rhythm also lie somewhere between 50 and 100 beats/min. Note that the fourth heart rate plot of the patient with AF is similar to the patients in normal sinus rhythm, albeit with more rate variability than is probably desirable. Nonetheless, it demonstrates that, with experience, clinicians can identify reasonable 24-hour heart rate graphs and use this as a starting point when applying a rate control strategy for their patient in AF.

Figure 5 provides an illustration of the impact of rate-control treatment on 24-hour heart rate in a patient with persistent AF considered suitable for rate-control therapy and anticoagulation. As the pretreatment plot shows, the patient’s heart rate often exceeds 100 beats/min for periods of several hours. With just a small dose of long-acting metoprolol, heart rate is brought under better control. This patient felt much better and became nearly asymptomatic. The advantage of this approach is that rate control is evaluated in the patient’s “natural” environment of routine activity, in which patients define their own level of activity. It makes little sense to me to judge rate control by exercise testing in a sedentary patient with AF. In fact, this can lead to over-medication. For example, the dosage of AV node blockers needed to control exercise heart rate may reduce resting heart rate so low that a pacemaker may mistakenly be thought necessary.

**Conclusions**

Recent clinical trials that compared strategies of rhythm control with rate control in patients with AF have demonstrated equivalence in terms of primary outcome measures, including mortality, but lacked information about the best appropriate endpoints for determining “successful” rate or rhythm control in individual patients. A reasonable endpoint for rhythm control is a marked reduction in the frequency and duration of symptomatic AF episodes. With few exceptions, most patients can live comfortably with occasional episodes of AF; it is not essential to eliminate all episodes of AF in order for therapy to be considered successful. For rate control, a 24-hour heart rate that mimics normal sinus rhythm is a reasonable endpoint. Achieving good rate control is essential to minimize symptoms and the risk of tachycardia-mediated cardiomyopathy.
References


