Rhythm or rate control in persistent atrial fibrillation

Peter G. Guerra, Denis Roy

Department of Medicine and Research Center, Montreal Heart Institute, Montreal, Quebec, Canada

Selecting appropriate treatment strategies for patients with persistent atrial fibrillation has often proved to be a quandary. Foregoing any debate on anticoagulant therapy, the remaining issue is whether the ultimate goal should be achieving and maintaining sinus rhythm or simply controlling the ventricular response during ongoing atrial fibrillation. Since atrial fibrillation affects 5% of the population over the age of 60 and increases with advanced age, it is a question of utmost clinical relevance [1]. Atrial fibrillation may be classified as paroxysmal, persistent, or chronic. Paroxysmal atrial fibrillation can be defined as AF which is self-limited, converting spontaneously to sinus rhythm; persistent AF is defined as necessitating an electrical or chemical cardioversion; whereas permanent or chronic AF does not respond to these maneuvers. For the purposes of this article, the focus will be on the treatment of persistent atrial fibrillation, as it is the subset which most often will require interventions to restore and maintain sinus rhythm.

Persistent atrial fibrillation can be asymptomatic, but it is often associated with symptoms of palpitations, dyspnea and chest pains. Angina and congestive heart failure can be precipitated or aggravated by atrial fibrillation. Rapid ventricular rates during atrial fibrillation may even engender a form of cardiomyopathy, which usually shows complete recovery after adequate control of the arrhythmia. Unfortunately, the most feared complication of atrial fibrillation is not as reversible. Atrial fibrillation accounts for approximately 80,000 strokes per year in the United States [1]. The benefits of anticoagulation in this population are well known, but it has often been hoped that rigorous maintenance of sinus rhythm might obviate the need for this cumbersome treatment, forming a cornerstone for the argument in favor of rhythm control. As the Framingham data suggests, atrial fibrillation also confers a 1.5 to 1.9 fold higher risk of mortality independent of other cardiovascular diseases [2]. These incapacitating symptoms and serious complications underscore the importance of identifying the best approach to treating this frequently-encountered arrhythmia.

The rhythm control strategy is appealing as it attempts to avert both the symptoms and the potential complications of the disease by maintaining sinus rhythm. However, this strategy can be complex in its execution as patients with persistent atrial fibrillation require a cardioversion to restore sinus rhythm. Success rates for electrical cardioversion vary from 79 to 94% depending on the amount of energy utilized and the manner in which it is delivered. Chemical cardioversion, although more simple to perform because no anesthesia is required, has less impressive success rates (with Class I agents being most effective) [3]. Regardless of how sinus rhythm is achieved, a rhythm control strategy may require multiple cardioversions, as atrial fibrillation will often recur.

The maintenance of sinus rhythm between intervening cardioversions necessitates pharmacologic or non-pharmacologic treatments.

Class I and III anti-arrhythmic agents have proven beneficial in this regard [4]. A meta-analysis demonstrated that quinidine resulted in twice as many patients remaining in sinus rhythm after one year. However, it also heralded the dangers of anti-arrhythmic therapy, as there was a three-fold increase in mortality in the quinidine group. Class I agents such as flecainide and propafenone were subsequently shown to have at least equal efficacy and better tolerability than quinidine [1]. Despite this, only approximately 50% of patients remain in sinus rhythm after one year. Some uncontrolled studies suggested that amiodarone might fare better in maintaining sinus rhythm, so this hypothesis was tested in the Canadian Trial of Atrial Fibrillation [5]. This study demonstrated a superior efficacy for amiodarone, with a 16-month follow-up showing that 65% of patients on amiodarone remained free of atrial fibrillation, compared to 37% of patients on sotalol and propafenone.

Concern over potential adverse effects has always weighed against anti-arrhythmic drug use. In particular, the
In certain cases, appropriate rate control cannot be achieved using only pharmacologic therapy, and in these cases, exercise. The doses of these medications need to be titrated to achieve the target response.

Digoxin, however, provides less adequate rate control during exercise. Beta-blockers and digoxin is preferable in patients with heart failure, whereas calcium antagonists are more appropriate for patients with pulmonary disease. These target heart rates are usually achieved with medical therapy. Beta-blockers, calcium channel blockers and digoxin, either alone or in combination have proved effective in achieving rate control. Utilization of beta-blockers and digoxin, either alone or in combination have proved effective in achieving rate control. The site of earliest activation within each vein. Pappone and colleagues showed that PV isolation could be performed using a three-dimensional electroanatomic mapping system. Circumferential lesions were made in the left atrium at a distance from the PVs. This technique provided a success rate of 80% at 10 months. Interestingly, recurrence rates were less in patients who had a larger ablation area, raising the possibility that elimination of PV triggers combined with reduction of atrial mass provided additional benefit. To date, these techniques remain somewhat difficult to perform, but as their utilization becomes widespread, they may prove to be interesting additions to the more common rhythm control methods.

In contrast to rhythm control, rate control has frequently been viewed as a therapy of resignation, reserved only for patients in whom rhythm control had proved to be unfeasible. Nonetheless, this strategy has the advantage of providing symptom relief and preventing tachycardia-induced cardiomyopathy without necessitating anti-arrhythmic medications. However, in order for rate control to be effective, it must achieve certain target heart rates both at rest and during exercise. Current recommendations suggest that the goal of therapy should be ventricular rates of 60–80 beats per minute at rest and 90–115 during exercise.

These target heart rates are usually achieved with medical therapy. Beta-blockers, calcium channel blockers and digoxin, either alone or in combination have proved effective in achieving rate control. Utilization of beta-blockers and digoxin is preferable in patients with heart failure, whereas calcium antagonists are more appropriate for patients with pulmonary disease. Digoxin, however, provides less adequate rate control during exercise. The doses of these medications need to be titrated to achieve the target response. In certain cases, appropriate rate control cannot be achieved using only pharmacologic therapy, and in these instances, ablation of the atrioventricular (AV) node with pacemaker implantation should be considered. In this manner, both rapid rates and abrupt changes in rhythm are avoided. Initially, Scheinman et al described ablation of the atrioventricular junction with DC shocks for patients with refractory supraventricular tachycardias. Refinement of this technique in subsequent years involved the development of catheters capable of delivering radiofrequency energy instead of DC shocks in order to perform the ablation. This method proved to be more efficacious than DC catheter ablation, with success rates as high as 97% for achieving complete AV block, and this new form of energy delivery did not produce the same type of barotrauma observed with both high and low DC shocks, explaining the trend towards less significant ablation complications such as early sudden death, ventricular arrhythmias or cardiac tamponade.

Current techniques have rendered the procedure successful in upwards of 98% of cases, with a low (1%) incidence of minor complications.

Despite current advances in catheter-based therapies for AF, AV nodal ablation and pacing remains a viable option for patients with drug-refractory AF for a number of reasons. Studies have shown that patients undergoing this procedure experienced a significant improvement in both quality of life indices and ease of activities of daily living. Fitzpatrick et al suggested that this improvement was more than subjective, as a significant reduction in doctor visits, hospital admissions and antiarrhythmic drug trials was documented in their 107 patients during the course of a 2 year follow-up. The procedure may be particularly useful in preventing congestive heart failure caused by the rapid ventricular rates during uncontrolled AF, and in certain cases, an improvement in left ventricular function may be noted after the procedure. Furthermore, despite previous concerns about rendering patients pacemaker dependent and possibly augmenting the risk of
Thus, both rhythm and rate control strategies carry with them multiple modalities and techniques with which to achieve the desired goal. Despite the potential adverse effects related to anti-arrhythmic therapy and the difficulties still encountered with curative ablation of atrial fibrillation, there exists a certain bias favoring rhythm control. There is an unquestionable allure in deploying efforts to achieve sinus rhythm, as many feel that this can alleviate symptoms, reduce the occurrence of heart failure, decrease the incidence of stroke and allow discontinuation of anticoagulants. Unfortunately, some of these assumptions are unfounded.

It is important to bear in mind that certain studies suggesting an improved quality of life during rhythm control strategies were performed in patients with paroxysmal, not persistent atrial fibrillation. Paroxysmal atrial fibrillation, particularly when the patient alternates between sinus rhythm and atrial fibrillation very frequently, can be as incapacitating as structural heart disease. However, symptoms associated with persistent atrial fibrillation are more often related to rapid ventricular rates, and there exists good evidence, particularly in the atrioventricular nodal ablation data [10] that rate control can be quite effective at providing symptom relief, as this method, more. As detailed by Fitzpatrick and colleagues, ensuring adequate rate control resulted in significant improvement of the quality of life index and the ease of activities of daily living. Improvement of symptoms, then, may not necessarily hinge on whether a rate or rhythm control strategy is employed, but rather may be dependent on successful implementation of those strategies.

Whereas rapid atrial fibrillation may precipitate acute congestive heart failure and cause ventricular dysfunction in the long term, both rhythm and rate control may be appropriate strategies for avoiding this complication. The merits of rhythm control are self-evident; but as previously stated, a well executed strategy of rate control can also confer reduction in emergency room visits, hospitalizations, and may reduce the progression to left ventricular dysfunction.

Maintenance of sinus rhythm is occasionally touted as method of stroke prevention, however, it can be difficult to evaluate the effectiveness of a rhythm control strategy, as episodes of atrial fibrillation are frequently asymptomatic. The advent of holter monitoring, implantable event recorders, and rhythm data collection on pacemakers and defibrillators has also brought to light the importance of this phenomenon. Thus, it may be imprudent to discontinue anticoagulation in higher risk patients based simply on their lack of symptoms, especially since it is well established that the risk of stroke is equivalent in patients with paroxysmal and persistent atrial fibrillation [1]. Van Gelder and colleagues showed that patients treated with a rhythm control strategy had more frequent thromboembolic events that patients treated with rate control. Notably, of 21 patients with this complication, anticoagulant therapy had been stopped in 6 and 5 patients were in sinus rhythm at the time of the event [10]. The desire to cease anticoagulation is therefore not a compelling argument in favor of rhythm control.

Recently, two major randomized control clinical trials compared the relative benefits of rhythm and rate control in the management of atrial fibrillation. The aforementioned Van Gelder study and the AFFIRM study [11] prospectively enrolled patients into each of the two treatment strategies. The European trial assigned 256 to rate control and 266 patients to rhythm control. The end point for this study was a composite of death from cardiac causes, heart failure, thromboembolic complications, bleeding, the need for a pacemaker, or serious adverse effects of the anti-arrhythmics. Twenty-two percent of patients in the rhythm control group reached the primary end point as compared to 17 percent in the rate control group, suggesting a trend favoring rate control. Of note, sinus rhythm was difficult to attain in this particular population, as 61% of patients in the rhythm control arm were in atrial fibrillation at the end of the study (90% in the rate control group). Thus, the majority of patients were subject to the risks of rhythm control while not necessarily achieving the possible benefits of sinus rhythm. The AFFIRM trial, though larger in scope, arrived at similar conclusions.

The primary endpoint in this trial was overall mortality and was non-significantly higher in the rhythm control group (356 patients) than in the rate control group (310 patients). There was a much higher success for achieving sinus rhythm in this study, with its prevalence being 82.4%, 73.3% and 62.6% at 1, 3, and 5 years respectively. A total of 248 patients crossed over from rate to rhythm control, most often due to excessive symptoms of atrial fibrillation or heart failure. However, 594 patients crossed over from rhythm to rate control due to side effects of the medications or simple inability to maintain sinus rhythm. This study did not demonstrate any differences in quality of life indices between the two groups.

It appears, then, that rate control is at least equivalent to rhythm control in terms of symptoms, serious complications, and mortality; although several important points were not addressed in these last two clinical trials. Both studies included only patients with previous episodes of atrial fibrillation, leaving open to debate whether a more conservative approach of rate control is appropriate in patients with a first episode of atrial fibrillation.
fibrillation who may have less propensity for recurrence. It also remains unclear whether non-pharmacologic methods of rhythm control such as pulmonary vein isolation may be of more benefit than the standard pharmacologic approach that was compared to rate control in these trials. Finally, one specific subset of patients, underrepresented in AFFIRM, are often felt by clinicians to require the additional contribution to cardiac output afforded by the atrial kick: those with congestive heart failure. The question of rate versus rhythm strategy in patients with heart failure is currently being addressed in a large multi-center trial [12].

Thus, while current data does not necessarily suggest we eschew any attempts at rhythm control for patients with persistent atrial fibrillation, it does exhort us to be more judicious in applying this strategy, particularly when recurrences are frequent and efforts at maintaining sinus rhythm appear ineffective.

References


Top

Updating: 10/15/2003