

ATRIAL FIBRILLATION: Rate Versus Rhythm Control

The management of atrial fibrillation has not only been a topic of intense debate and clinical investigation in recent years, but it is also becoming more frequent due to an aging population and increasing risk factors for the development of atrial fibrillation. The incidence of atrial fibrillation increases with age. Approximately 1.7 – 3.0% of patients between the ages of 65-69 will have atrial fibrillation and this will increase to more than 10% of those greater than 85 years of age¹. The Framingham Heart Study noted a five fold increase in the risk of stroke and embolic events in those with atrial fibrillation. Atrial fibrillation is responsible for approximately 15% of strokes in the United States. Chronic atrial fibrillation and paroxysmal atrial fibrillation (PAF) appear to carry the same degree of risk for stroke.¹ Although the risk of stroke and embolic events also increases with age, other clinical factors (Figure 1) increase the risk of an embolic event at all age levels. For example, patients with complex aortic plaque on transesophageal echocardiography have a risk of thromboembolism of 12% per year compared with a risk of stroke of 1.3% per year in patients without this abnormality¹. With numerous medical options and the advent of newer invasive procedures for the treatment of atrial fibrillation, what is the best approach in the treatment of this disorder?

While the maintenance of normal sinus rhythm has long been the established ideal, several recent studies have suggested that rate control may well be preferable to rhythm control in the majority of patients with atrial fibrillation. As noted in Figure 2, the stroke rates in four “rate versus rhythm trials” have all shown that the stroke rate is the same as, or perhaps even slightly higher, in the rhythm control group compared with the rate control group. This is likely a result of the fact that in rhythm control, recurrence of atrial fibrillation has been documented by transtelephonic monitoring in up to two-thirds of patients. Up to 70% of such individuals with paroxysmal atrial fibrillations are asymptomatic and unaware of these recurrent events. Thus, antiarrhythmic therapy seems poorly effective in maintaining sinus rhythm and is associated with a high incidence of often asymptomatic periods of paroxysmal atrial fibrillation. Paroxysmal atrial fibrillation seems to be a risk factor for embolic events as frequently as it is in permanent atrial fibrillation, therefore there should probably be a low threshold for continuing Warfarin therapy indefinitely in the large proportion of patients with a history of atrial fibrillation, even when antiarrhythmic therapy is used. In addition, of the armamentarium of antiarrhythmic drugs, most are associated with significant side effects. The use of Class 1c agents, such as Flecainide and Propafenone, for example, have been associated with an increased risk of sudden death in patients with prior myocardial infarction and are contraindicated in patients with atrial fibrillation and ischemic heart disease. The presence of left ventricular hypertrophy also seems to increase the risk for ventricular arrhythmias when this class of drugs are used. Amiodarone, perhaps the most effective antiarrhythmic agent, has a discontinuation rate of 18% of patients over a 16 month period and up to 40% of patients will discontinue the use of Amiodarone within two years because of side effects^{2,3}. Nearly 40% of the molecular weight of Amiodarone is iodine, and in addition to the well known side effects of hyper and hypothyroidism, iodine can also penetrate into other tissues and has been associated with other organ toxicities such as congestive and inflammatory hepatopathy.

Skin deposits, photosensitivity, peripheral neuropathy, and tremors are additional side effects. Optic neuritis, though a rare complication, may occur after the first dose and is irreversible³. Two forms of pulmonary toxicity may occur; one, an inflammatory idiosyncratic condition, may occur after 2-3 weeks of Amiodarone dosing and is manifested by cough, fevers, and acute respiratory decompensation. Pulmonary fibrosis may occur after longer periods of time when patients have been on Amiodarone for many years. Thus, not only are there limitations to several of the antiarrhythmic medications, but the most effective agent has numerous side effects associated with acute or long-term usage. Catheter ablation of atrial fibrillation – more appropriately termed catheter based isolation of pulmonary veins – has been an increasingly popular procedure to treat patients with symptomatic atrial fibrillation. Despite the promise of a more permanent solution, in a recent review⁴, the antiarrhythmic free success rate following pulmonary vein isolation approximately one year following ablation was only 52% and was associated with at least one major complication in 6% of the patients. A review from the University of Michigan comprising 800 patients noted a three year success rate following catheter ablation of 80% in patients with paroxysmal atrial fibrillation and 70% in those with chronic atrial fibrillation⁵. A 70-80% cure rate is certainly not high in comparison with a cure rate of nearly 99% for other arrhythmias treated with ablation technology such as WPW or PSVT caused by AV node re-entry. In addition, it appears that pulmonary vein isolation therapy for atrial fibrillation probably does not eliminate the need for chronic Coumadin therapy since it is not yet known to what extent paroxysmal atrial fibrillation occurs after this procedure, and at least some studies suggest that PAF occurs in a significant number of patients⁶. The University of Michigan's database also has shown that close to 20% of their patients develop left atrial flutter post ablation and 5% of these patients have needed a second procedure to treat flutter.

In those individuals who are rate controlled, the issue over and above an effective anticoagulation regimen with the goal of achieving an INR from 2.0-3.0, is to assure truly adequate rate control. Three classes of drugs are used for this purpose. Digoxin, beta blockade therapy, and non-dihydropyridine calcium channel blockers (Verapamil and Diltiazem). Digoxin is usually not a suitable medication for achieving rate control - especially during exercise - compared with beta blockade therapy and non-dihydropyridine calcium channel blockers. The importance of assuring adequate control of the ventricular response during atrial fibrillation is essential in preventing a rate induced cardiomyopathy. Also, since atrial fibrillation occurs in patients with other risk factors associated with diastolic dysfunction (hypertension, coronary artery disease, valvular heart disease) slowing of the ventricular response and increasing the length of diastole is important in preventing the symptoms of dyspnea that may also occur with diastolic abnormalities as well. Finally, aspirin alone (compared with placebo) reduces the risk of thromboembolism in atrial fibrillation by only about 22%, whereas Coumadin provides a 45% decrease in all strokes and a 52% decrease in ischemic strokes compared with aspirin. An oral thrombin inhibitor, Ximelagatran, was not approved by the FDA for use in atrial fibrillation after the SPORTIF studies demonstrated significant hepatotoxicity with this agent.

In conclusion, it would appear that in many patients with chronic atrial fibrillation – especially more elderly patients with multiple co-morbid factors noted in Figure 1 - a strategy of rate control and Warfarin anti-coagulation may be ideal because of the simplicity, effectiveness, and safety of this approach. Attention should be directed at truly achieving rate control, either by performing in office response to moderate exercise (walking up or down a flight of stairs), or probably more effectively with a 24 hour Holter monitor with unrestricted activity. Pulmonary vein isolation in experienced centers may be an option in probably younger selected patients who are symptomatic or unresponsive to drug therapy. In those individuals that have not responded to rate control, the effective therapy of AV node ablation and pacemaker placement serves as an option in individuals who are at risk for developing tachycardia induced cardiomyopathy or symptoms related to diastolic abnormalities.

REFERENCES

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Risk Factors For Stroke With Atrial Fibrillation

Age > 65

Prior stroke

Diabetes mellitus

Hypertension

Left atrial enlargement

Left ventricular dysfunction

Significant aortic plaque burden on TEE

Coronary artery disease

Valvular heart disease

Left ventricular hypertrophy