Rate Versus Rhythm Control for Atrial Fibrillation

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KEYWORDS

• Rate • Rhythm • Atrial fibrillation • Heart

KEY POINTS

- Treatment of patients with symptomatic atrial fibrillation (AF) with antiarrhythmic drug therapy in general improves their symptom scores and exercise tolerance; however, large randomized trials have failed to show a mortality benefit with a rhythm-control compared with a rate-control strategy.
- Catheter ablation in patients who have failed or not tolerated medical therapy has been shown to alleviate symptoms and improve quality of life.
- At experienced centers, the risk of a serious procedure-related complication should be low.
- Patients should be alerted to modifiable factors that may decrease the likelihood of unchecked structural remodeling and AF recurrence, such as obesity, sleep apnea, and hypertension.
- Given the increasing incidence of AF, upstream therapies that might prevent AF are urgently needed.

Atrial fibrillation (AF) is a progressive disease that continues to inflict a heavy burden on health care systems and patients. AF portends an increased all-cause mortality, long-term stroke risk, heart failure, and impaired quality of life (QoL).[1–4] Goals of treatment include symptom alleviation, stroke prevention, and identifying modifiable factors that may be contributing to the fibrillatory process, such as obesity, hypertension, and sleep apnea. Medical treatment intended to improve symptoms referable to AF includes rate-controlling medications (rate-control strategy), and antiarrhythmic drugs (AADs) (rhythm-control strategy). Nonpharmacologic options include atrioventricular (AV) junction ablation/permanent pacemaker implantation and catheter ablation to maintain sinus rhythm, respectively. This article reviews the evidence base for the rate-control and rhythm-control strategies and proposes a practical approach in managing patients with AF.

DRUG THERAPY FOR MAINTENANCE OF SINUS RHYTHM

Before discussing trials that have compared rhythm-control and rate-control strategies, a review of the evidence base of each is worthwhile. In the Canadian Trial of Atrial Fibrillation, patients with symptomatic paroxysmal or persistent AF were randomized to amiodarone, sotalol, or propafenone.[1] Rhythm status was ascertained with an electrocardiogram at 3 months, and then every 6 months thereafter. After a mean follow-up of 16 months, 35% of patients who were assigned to amiodarone and 63% of those to either sotalol or propafenone experienced recurrent AF

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(*P*<.001). Drug discontinuation because of adverse effects was noted in 18% of patients randomized to amiodarone versus 11% of those to either sotalol or propafenone (*P* = .06). In the Sotalol Amiodarone Atrial Fibrillation Efficacy Trial (SAFE-T), patients with persistent AF were randomized to amiodarone, sotalol, or placebo.[2] Rhythm status was assessed with weekly transtelephonic monitoring. The median times to recurrence were 487, 74, and 6 days, respectively. The recurrence rates at 1 year were 48%, 68%, and 87%, respectively. Maintenance of sinus rhythm was associated with an improved QoL and exercise tolerance. Although amiodarone has been shown to be superior in other trials, a high dose of the drug (300 mg per day for the first year after a loading dose) was used in the SAFE-T study. Both study drugs were well tolerated.

Even though amiodarone is probably the most effective antiarrhythmic medication available, its effect is still modest. Further, its potential for end-organ toxicity is also limiting. Class IC agents such as propafenone and flecainide are best avoided in patients with structural disease, such as prior myocardial infarction, heart failure, and significant left ventricular hypertrophy. Given these limitations of both amiodarone and class I drugs, other agents have been introduced that could safely be used in patients with heart disease. The efficacy of dofetilide, a class III antiarrhythmic medication that blocks the delayed rectifier potassium channels (IK_r) channel, was tested in more than 1500 patients with systolic heart failure in the Danish Investigations of Arrhythmia and Mortality on Dofetilide Study Group.[3] The investigators noted a lower incidence of AF and hospitalizations in the group randomized to dofetilide. There was no difference in mortality between the dofetilide and placebo groups. However, torsades de pointes was observed in 3.3% of patients randomized to drug therapy. A substudy later revealed that, in a subgroup of 506 patients with atrial arrhythmias at baseline, those randomized to dofetilide were more likely to maintain sinus rhythm at 1 year compared with those randomized to placebo (79% vs 42%; *P*<.001).[4] There was no effect on mortality but survival was enhanced in those who maintained sinus rhythm.

A major limitation of dofetilide is that it requires in-hospital initiation because it prolongs ventricular repolarization and may cause torsades de pointes. Dose reduction is often required because of QT prolongation (**Fig. 1**). The potential for drug-drug interaction (eg, with various antibiotics, thiazide diuretics, and verapamil) is also limiting.

Despite its superior efficacy compared with other antiarrhythmics, amiodarone is rarely used as a first-line agent because of the concern of end-organ toxicity. The adverse effects are thought to be related to its iodine content. And thus dronedarone, which is devoid of the iodine moiety, was introduced in hopes of maintaining the efficacy of amiodarone but without its adverse effects on the lungs, liver, and thyroid. In a multicenter clinical trial, 1237 patients with paroxysmal or persistent (after cardioversion) AF

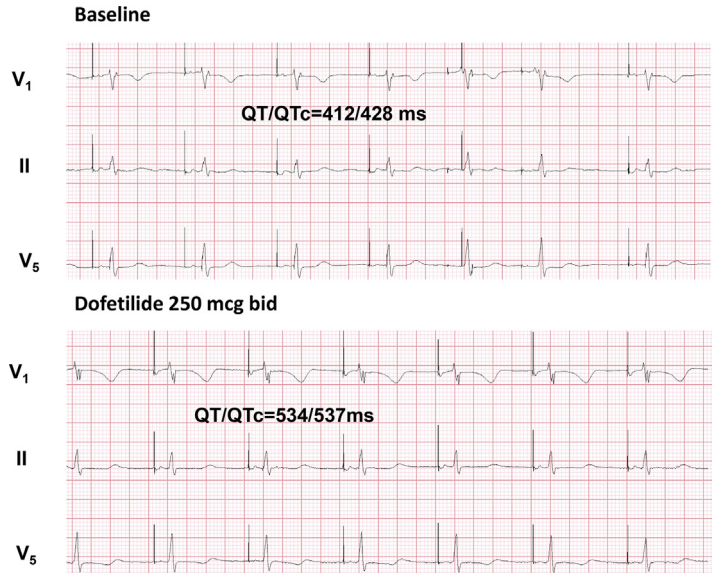

Fig. 1. Prolonged repolarization after initiation of dofetilide. The baseline rhythm is atrial pacing with intrinsic AV nodal conduction. Owing to prolongation of the QT interval and ventricular ectopy (not shown), dofetilide was discontinued and the patient underwent catheter ablation of persistent AF. BID, twice a day.