Recurrent AF: Choosing the Right Medication.

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Introduction:
Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting an estimated 2.3 million people in North America. The estimated prevalence is 0.4% to 1% in the general population and up to 8% in the population > 80-years-of-age. AF is associated with an increased risk of stroke and all-cause mortality, although it is unclear whether this is a marker of severity of underlying heart disease or whether there is a causative relationship.

AF may have a wide spectrum of presentations and associations. Patterns of arrhythmia presentation may include:

- first-detected episode,
- paroxysmal recurrent (recurring and spontaneously terminating within seven days),
- persistent recurrent (recurring and sustaining over seven days) and
- permanent (in which case restoration of sinus rhythm fails or is abandoned).

While some patients are entirely unaware that they have AF, others may be highly symptomatic from relatively brief episodes of paroxysmal AF. Treatment strategies may thus differ between patients based on their symptoms and risk of stroke. There are three important clinical targets for the treatment of AF:

1. Control of thromboembolic risk
2. Prevention of tachycardia-induced cardiomyopathy
3. Control of symptoms

AF may also be associated with numerous underlying cardiac and non-cardiac
conditions. This review will focus on treatment of recurrent AF, assuming underlying conditions have been treated separately.

Thromboembolic Prophylaxis:
The risk of thromboembolism is markedly increased by the presence of AF. Stroke risk may be predicted by clinical criteria, which guide therapy with either ASA or warfarin (Table 1). AF reduces atrial transport function, promoting the formation of left atrial thrombus, hence it is associated overall with an increase in the risk of embolic stroke. All patients with AF should be assessed regarding requirement for long-term anticoagulation (Table 2).

Rate control:
In the absence of atrioventricular (AV) nodal disease, most patients will have a rapid ventricular rate in the setting of AF. Tachycardia reduces ventricular filling time and increases heart work. Persistent tachycardia can result in deterioration of heart function—a condition known as tachycardia-induced cardiomyopathy. β-blockade or a non-dihydropyridine calcium channel antagonist (verapamil or diltiazem) and slow AV nodal conduction are recommended for rate control. Digoxin slows ventricular rate during AF mainly by increasing vagal tone and hence is effective for controlling rate at rest but is less effective during activity. However, it may be suitable for sedentary individuals or those with reduced ejection fraction. Combination therapy may be required in some patients. In some cases, a pacemaker may be required if necessary pharmacologic therapy for rate control is associated with excessive bradycardia, or when pharmacologic rate control cannot be achieved and AV node ablation is required.

AF with Wolff-Parkinson-White syndrome (WPW) and rapid ventricular preexcitation (which will have an ECG appearance of rapid irregular wide-complex tachycardia) is a special case in which AV node-blocking drugs (as above) may be deleterious and drugs such as procainamide or amiodarone should be used. Direct current (DC) cardioversion is often preferred to drugs in patients who have new-onset rapid AF and WPW.

There is limited data on how aggressively rate control should be pursued. Commonly accepted guidelines are based on the targets in the Atrial Fibrillation Fol-
low-up Investigation of Rhythm Management (AFFIRM) trial which aimed to achieve a resting heart rate of < 80 bpm, or an average heart rate of < 100 bpm on a 24 hour Holter monitor.

**Symptom control:**
There are two approaches to the treatment of AF. One is cardioversion and treatment with anti-arrhythmic drugs (Tables 3 and 4) (or catheter ablation) to maintain sinus rhythm; the other is the use of rate-controlling drugs (Tables 5 and 6), allowing AF to persist. The AFFIRM trial randomized patients with AF to either a rhythm- or rate-control strategy. The study found that management of AF with the rhythm control strategy offered no survival advantage, or other clear advantage over the rate-control strategy. The recently completed Atrial Fibrillation and Congestive Heart Failure (AFCHF) trial compared a strategy of rate-control to rhythm-control in patients with systolic heart failure and, again, found no advantage to rhythm-control.

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<th>Table 3</th>
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<td><strong>Rhythm control acute cardioversion</strong></td>
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<td><strong>Initial</strong></td>
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<td>Procainamide</td>
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<td>Propafenone</td>
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<th>Table 4</th>
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<tr>
<td><strong>Rhythm control maintenance</strong></td>
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<td><strong>Maintenance</strong></td>
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<td>Amiodarone</td>
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<td>Propafenone</td>
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<td>Flecainide</td>
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<td>Sotalol</td>
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*VT: Ventricular tachycardia*
The decision to use antiarrhythmic drugs is thus dependent on the patient's symptoms. While rate control may control symptoms for many patients, highly symptomatic individuals will often require treatment aimed at restoring or maintaining sinus rhythm. If the AF has been present for > 48 hours, attempts to restore sinus rhythm should be deferred until the patient has received anticoagulation for four weeks to avoid risk of stroke. These patients may be offered cardioversion without a month of prior anticoagulation if a trans-esophageal ECHO is able to exclude the presence of a left atrial thrombus. They will still require three to four weeks of anticoagulation post-cardioversion since the atria often do not immediately recover full mechanical function. Acute onset AF in patients without structural heart disease may be treated with flecainide, propafenone or ibutilide. All are associated with a risk of ventricular pro-arrhythmia, especially in patients with structural heart disease. For patients with structural heart disease, IV or oral amiodarone can be used.

Maintenance of sinus rhythm can be attempted with oral flecainide or propafenone if the patient does not have structural heart disease. As with acute administration, a risk of ventricular pro-arrhythmia exists. In those with structural heart disease, sotalol can be used with caution. This drug may prolong the QT interval and has a risk of torsades de pointes. Amiodarone is the most effective drug for maintenance of sinus rhythm but
is associated with multiple systemic side-effects including:

- thyroid disease,
- pulmonary fibrosis,
- peripheral neuropathy and
- liver dysfunction.

The patient should take the lowest dose effective at controlling symptoms.

**Take-home points:**

- All patients having recurrent episodes of AF should have their risk of stroke from the arrhythmia assessed. Long-term treatment with warfarin or ASA may be required depending on the patient’s risk profile

- The decision of whether to start antiarrhythmic treatment is based on the patient’s symptoms. Rate control is a reasonable first option for symptomatic therapy for most patients

- For patients who require rhythm control, antiarrhythmic medications should be considered carefully as each has a unique adverse effect profile

**References:**
