Recurrent AF:
Choosing the Right Drug

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Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia,[1,2] affecting an estimated 2.3 million people in North America. The estimated prevalence is 0.4% to 1% in the general population[3] and up to 8% in the population > 80-years-of-age.[4] AF is associated with an increased risk of stroke and all-cause mortality,[5] although it is unclear whether this is a marker of severity of underlying heart disease[6] 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).[1]

While some patients are entirely unaware that they have AF, others may be highly symptomatic from relatively brief episodes of paroxysmal AF.[7] 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

Table 1
Risk factors for stroke in the presence of atrial fibrillation (AF)[9]

High-risk factors	Moderate-risk factors
• History of stroke/TIA • Hypertension • Reduced LV function • Age > 75 years • Mitral stenosis • Prosthetic heart valve	• Age 65-75 years • Diabetes • Coronary artery disease without LV dysfunction

TIA: Transient ischemic attack
LV: Left ventricular

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).[8,9] AF reduces atrial transport function, promoting the formation of left atrial thrombus,

Table 2

Recommended therapy to reduce the risk of stroke in the presence of AF[9]

Risk factors	Recommended therapy
Any high-risk factor or > 1 moderate-risk factor	Warfarin (target INR 2.5, range 2.0-3.0)
1 moderate-risk factor	ASA 75-325 mg q.d. or Warfarin (target INR 2.5, range 2.0–3.0)
No high-risk factors and no moderate-risk factors	ASA 75–325 mg q.d.

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).

In the absence of atrioventricular nodal disease, most patients will have a rapid ventricular rate in the setting of AF.

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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. ß-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 pre-excitation (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 Follow-up Investigation

Table 3
Rhythm control acute cardioversion

	Initial	Notes
Procainamide	15 mg/kg, not faster than 50 mg/min	Must have rate control first, risk of *torsades de pointes*, 1:1 flutter, hypotension
Propafenone	600 mg	Must have rate control first, risk of 1:1 flutter, bradycardia
Flecainide	300-400 mg p.o.	Must have rate control first, risk of 1:1 flutter, bradycardia
Ibutilide	1 mg IV over 10 minutes, repeat after 10 minutes if necessary	Risk of *torsades de pointes*
Amiodarone	1g IV over 24 hours, then 400 mg b.i.d. for 1 week	Risk of hypotension, bradycardia

Table 4
Rhythm control maintenance

	Maintenance	Risks
Amiodarone	100-400 mg q.d.	Adverse effects to skin, lungs, nerves, GI, liver, thyroid and eyes, bradycardia, rarely *torsades des pointes*
Propafenone	150-300 mg t.i.d.	VT, heart failure, 1:1 flutter
Flecainide	50-150 mg b.i.d.	VT, heart failure, 1:1 flutter
Sotalol	40-160 mg b.i.d	*Torsades des pointes*, heart failure, bradycardia, asthma. Avoid use when QT is prolonged, or with hypokalemia, or concomitant diuretic use

VT: Ventricular tachycardia

of Rhythm Management (AFFIRM) trial[10] 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.[11]

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.[12] The recently completed Atrial Fibrillation and Congestive Heart Failure (AF-CHF) trial compared a strategy of rate-control to rhythm-control in patients with systolic heart

Table 5
Drugs for acute rate control in AF

Drugs	Initial dose	Maintenance dose
Metoprolol	2.5-5 mg IV max 15 mg	
Esmolol	500 mcg/kg IV over 1 min	60-200 mcg/kg/min
Diltiazem	0.25 mg/kg IV over 2 min	5-15 mg/hr IV
Verapamil	0.075-0.15 mg/kg IV	
With WPW and rapid pre-excited ventricular conduction*		
Procainamide	15 mg/kg IV, not faster than 50 mg/min	
Amiodarone	150 mg IV over 30 min	0.5-1 mg/min
With CHF		
Digoxin	0.25 mg IV q.2.h. up to 1.5 mg	0.125-0.375 mg q.d. IV/p.o.
Amiodarone	150 mg IV	0.5-1 mg/min

* Usually, DC cardioversion preferred
WPW: Wolff-Parkinson-White syndrome CHF: Congestive heart failure

Table 6
Drugs for chronic maintenance of rate control in AF

Drugs	Maintenance dose
Metoprolol	25-100 mg b.i.d.
Atenolol	25-100 mg q.d.
Diltiazem	120-480 mg q.d.
Verapamil	180-360 mg q.d.
Amiodarone (when others fail)	As below
With CHF	
Digoxin	0.125-0.375 mg q.d.

While rate control may control symptoms for many patients, highly symptomatic individuals will often require treatment aimed at restoring or maintaining sinus rhythm.

failure and, again, found no advantage to rhythm-control.[13]

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

- 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

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[14] 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. Dx

References
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2. Feinberg WM, Blackshear JL, Laupacis A, et al: Prevalence, Age Distribution and Gender of Patients with Atrial Fibrillation. Analysis and Implications. Arch Intern Med 1995; 155(5):469-73.

For more references, please contact **diagnosis@sta.ca**.