

# Practical Management of Atrial Fibrillation

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Adapted from the AHA/ACC/HRS  
2014 Guideline for the Management  
of Patients with Atrial Fibrillation

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## EPIDEMIOLOGY

- AF is the most common sustained arrhythmia encountered in clinical practice.
- Prevalence: 0.4% to 1% in general population, increasing with age to 12% for those > 75 yrs.
- Stroke rate: < 1% to > 15% annually, depending on comorbid risk factors.

## PATHOPHYSIOLOGY

- AF may be triggered by a focal source of rapid atrial electrical depolarization, often in the pulmonary veins. It is sustained by the presence of multiple reentrant wavelets or spiral wave re-entrant circuits (rotors).

## RELATED CONDITIONS

- AF may be triggered by acute, temporary causes including alcohol intake (“holiday heart syndrome”), surgery (particularly cardiac surgery), electrocution, MI, pericarditis, myocarditis, pulmonary embolism, or hyperthyroidism. In these cases, concurrent treatment of the underlying disorder and management of AF with a short course of AV nodal blocker or antiarrhythmic medication usually results in termination of AF without recurrence.
- AF may also be triggered by other arrhythmias, such as atrial tachycardia or flutter, Wolff-Parkinson-White (WPW) syndrome, or AV nodal reentrant tachycardia. Treatment of the triggering arrhythmia may prevent future AF episodes.
- AF may also be associated with chronic disorders, such as HF, sleep apnea, hypertension, and obesity. Treatment of these related conditions may ameliorate or eliminate AF.

## General Approach to the Patient with AF

### 1. Establish an Accurate Diagnosis of AF

- AF is characterized by uncoordinated atrial activation with consequent deterioration of atrial mechanical function. Consistent P waves are replaced by fibrillatory waves, which vary in amplitude, shape, and timing.
- The ventricular response is irregular and frequently rapid when AV nodal conduction is intact.
- Electrocardiogram (ECG) documentation is needed to confirm the diagnosis of AF. The ECG should also be evaluated for preexcitation (WPW), prior MI, or other atrial arrhythmias.
- An event recorder may be useful to correlate symptoms with the rhythm and determine the classification of AF.
- In patients with a pacemaker or a defibrillator, diagnosis of AF may require temporary inhibition or interrogation of the device to expose atrial activity.
- AF should be distinguished from 1) atrial flutter, which has regular organized atrial activity with an atrial rate typically between 240 and 320 bpm; 2) multifocal atrial tachycardia, which has 3 or more distinct P waves of variable morphology; 3) regular supraventricular tachycardias, such as AV nodal reentry; and 4) sinus rhythm (SR) with multiple premature atrial complexes.

### 2. Evaluation: Determine AF Classification, Clinical History, and Symptoms

#### AF is classified as:

- Paroxysmal: AF that terminates spontaneously or with intervention within 7 days of onset.
- Persistent: Continuous AF that is sustained > 7 days.
- Longstanding persistent: Continuous AF of > 12 months duration.
- Permanent: Permanent AF is used when there has been a joint decision by the patient and clinician to cease further attempts to restore and/or maintain sinus rhythm. Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician, rather than an inherent pathophysiological attribute of AF. Acceptance of AF may change as symptoms, the efficacy of therapeutic interventions, and patient and clinician preferences evolve.
- Nonvalvular AF: AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.

## Medical history should include:

- Onset of the first symptomatic attack or date of discovery of AF.
- The onset of the current episode, if persistent.
- Presence and severity of symptoms associated with AF.
- Frequency, duration, precipitating factors, and modes of termination of AF.
- Presence of other symptoms that might indicate an etiology.
- History of prior evaluation and response to prior management (i.e., pharmacological agents or cardioversion).
- Identification of thromboembolic and bleeding risks.

## 3. Assess for Structural Heart Disease

- Patients who initially present with AF should be evaluated for concomitant structural heart disease. The presence or absence of heart disease will help to individualize AF management.
- Transthoracic echocardiogram (TTE) should be performed to identify valvular heart disease, LA and RA size, LV size and function.
- Coronary artery disease should be excluded in patients with risk factors, but is rarely a reversible cause of AF.
- Severe left atrial dilation correlates with a low likelihood of maintenance of SR.

## 4. Identify Correctable Secondary Causes

- Identify and treat any potentially correctable causes such as sleep apnea, hyperthyroidism, WPW, and drug or alcohol abuse.

## 5. Develop a Treatment Strategy

### General Principles

- A comprehensive treatment plan must address the three cornerstones of AF management: 1) prevention of thromboembolism, 2) rate control, and 3) rhythm control.
- Hospitalization should be considered in patients who are significantly symptomatic, hemodynamically unstable, or being started on an antiarrhythmic drug.
- Electrical cardioversion can be performed as an outpatient procedure.
- When the cause of AF is reversible, such as AF after cardiac surgery, no long-term therapy may be necessary.
- Patients being treated by a cardiologist who continue to be symptomatic or are difficult to manage should be referred to an electrophysiologist.

## Acute Treatment Principles

### For hemodynamically unstable patients:

- Sedate if possible and perform an immediate cardioversion.
- If refractory to cardioversion, use IV amiodarone, ibutilide, or procainamide.

### For hemodynamically stable patients:

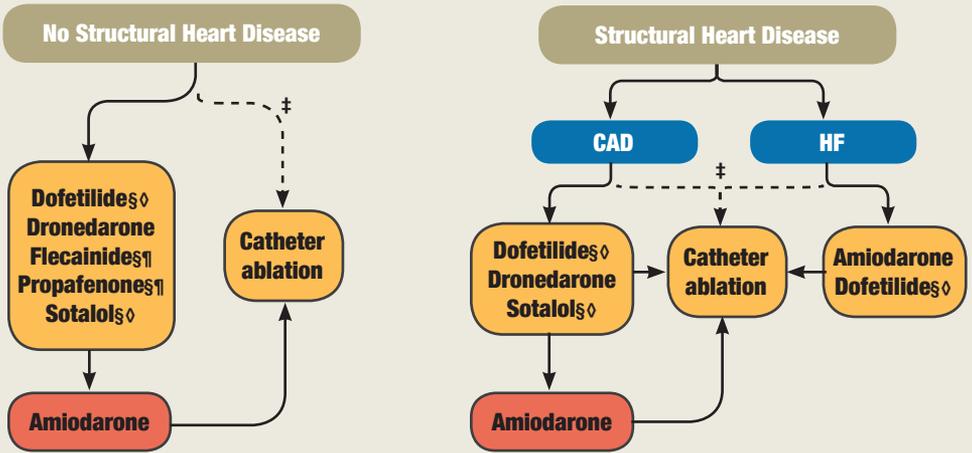
- Initiate anticoagulation and rate control.
- If first occurrence, consider cardioversion after adequate anticoagulation (4 weeks) or no clot seen on TEE and therapeutic anticoagulation initiated.
- With recurrence, consider referral to an electrophysiologist.
- Consider admission if history suggests a precipitating event (e.g., acute MI, PE, HF, etc.).
  - Rule out secondary causes (listed above) based on history.
  - Perform evaluation as stated above.

## Long-Term Treatment Principles

### Stroke Prevention

- AF is an independent risk factor for stroke.
- Antithrombotic therapy to prevent thromboembolism should be considered for all patients with AF—regardless of whether a rhythm or rate control strategy is chosen, except for those with contraindications.
- Patients with AF who have hypertrophic cardiomyopathy, mitral stenosis, or a mechanical valve should be treated with warfarin regardless of the presence or absence of other risk factors.
- The CHA<sub>2</sub>DS<sub>2</sub>-VASc scoring system is recommended to risk-stratify patients with nonvalvular AF to determine the need for anticoagulation therapy.
- Long-term oral anticoagulation (warfarin, factor Xa inhibitor, or direct thrombin inhibitor) is indicated in patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of  $\geq 2$ .
- For patients at low risk of stroke (CHA<sub>2</sub>DS<sub>2</sub>-VASc = 1), the physician may consider no anticoagulation, anticoagulation, or use of aspirin depending on patient priorities (stroke prevention vs. fear of a major bleed).
- Antithrombotic therapy recommendation is the same for patients with atrial flutter as for those with AF.
- There are several bleeding risk tools available, e.g., HAS-BLED, HEMORR<sub>2</sub>HAGES, ATRIA, etc. There is insufficient evidence to recommend one bleeding risk tool over another.

## Strategies for Rhythm Control in Patients with Paroxysmal\* and Persistent AF†



\* Catheter ablation is only recommended as first-line therapy for patients with paroxysmal AF (Class IIa recommendation).

† Drugs are listed alphabetically.

‡ Depending on patient preference when performed in experienced centers.

§ Not recommended with severe LVH (wall thickness > 1.5 cm).

◇ Should be used with caution in patients at risk for torsades de pointes ventricular tachycardia.

‡ Should be combined with AV nodal blocking agents.

Dronedarone is contraindicated in patients with congestive heart failure.

AF: atrial fibrillation; CAD: coronary artery disease; HF: heart failure; and LVH: left ventricular hypertrophy.

- The selection of antithrombotic should be based on shared decision making with patients that takes into account several factors, including patient risk factors and preference, tolerability, potential drug interaction, and cost.
- Aspirin monotherapy or aspirin plus clopidogrel are not substitutes for warfarin or the newer oral antithrombotic agents.
- For patients who are at high risk of thromboembolism, the performance of some procedures, including pacemaker and defibrillator implantation, is safer when performed on uninterrupted warfarin compared to bridging with heparin.
- Periodic re-evaluation of stroke and bleeding risk is recommended.

Risk Category	Recommended Therapy
No risk factors	It is reasonable to omit antithrombotic therapy or aspirin
1 point	No anticoagulant or treatment with an anticoagulant or aspirin may be considered
2 or more points	Oral anticoagulant*

\*If warfarin is the oral anticoagulant used, INR should be 2.0 to 3.0, with a target of 2.5. INR < 2.0 is not effective at preventing strokes. If mechanical valve, target INR > 2.5.

CHA <sub>2</sub> DS <sub>2</sub> -VASc Risk Criteria	Points
Congestive Heart Failure/LV Dysfunction	1
Hypertension	1
Age ≥ 75 Years	2
Diabetes Mellitus	1
Prior Stroke, TIA, thromboembolism	2
Peripheral Vascular Disease or Coronary Artery Disease	1
Age 65-74 Years	1
Sex Category (i.e., Female Sex)	1

Score	Adjusted stroke rate (%/year) based on CHA <sub>2</sub> DS <sub>2</sub> -VASc score
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	6.7
9	15.2

## Dose Selection of Oral Anticoagulant Options for Patients with Nonvalvular AF and CKD (Based on Prescribing Information for the United States)\*

Renal Function	Warfarin	Dabigatran†	Rivaroxaban†	Apixaban†
<b>Normal/Mild Impairment</b>	Dose adjusted for INR 2.0–3.0	150 mg BID (CrCl >30 mL/min)	20 mg QD with the evening meal (CrCl >50 mL/min)	5.0 or 2.5 mg BID‡
<b>Moderate Impairment</b>	Dose adjusted for INR 2.0–3.0	150 mg BID or 75 mg BID§ (CrCl >30 mL/min)	15 mg QD with the evening meal (CrCl 30–50 mL/min)	5.0 or 2.5 mg BID‡
<b>Severe Impairment</b>	Dose adjusted for INR 2.0–3.0◊	75 mg BID§ (CrCl 15–30 mL/min)	15 mg QD with the evening meal (CrCl 15–30 mL/min)	No recommendation¶
<b>End-Stage CKD Not on Dialysis</b>	Dose adjusted for INR 2.0–3.0◊	Not recommended¶ (CrCl <15 mL/min)	Not recommended¶ (CrCl <15 mL/min)	No recommendation¶
<b>End-Stage CKD on Dialysis</b>	Dose adjusted for INR 2.0–3.0◊	Not recommended¶ (CrCl <15 mL/min)	Not recommended¶ (CrCl <15 mL/min)	5.0 or 2.5 mg BID¶#

\* Renal function should be evaluated prior to initiation of direct thrombin or factor Xa inhibitors and should be reevaluated when clinically indicated and at least annually. CrCl should be measured using the Cockcroft-Gault method.

† The concomitant use of P-glycoprotein inducers or inhibitors with dabigatran, or the concomitant use of dual P-glycoprotein and strong CYP3A4 inducers or inhibitors with either rivaroxaban or apixaban, particularly in the setting of CKD, may require dosing adjustment or avoidance of concomitant drug use (see the FDA drug label at [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2014/202155s002lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/202155s002lbl.pdf); Section 8.6).

‡ Use apixaban 2.5 mg BID if any 2 patient characteristics present: Cr  $\geq$ 1.5 mg/dL,  $\geq$ 80 years of age, body weight  $\leq$ 60 kg. Apixaban is not recommended in patients with severe hepatic impairment.

§ Modeling studies suggest that dabigatran 75 mg BID might be safe for patients with CrCl 15–30mL/min, but this has not been validated in a prospective cohort. Some countries outside the United States use 110 mg BID.

◊ Dose-adjusted warfarin has been used, but observational data regarding safety and efficacy are conflicting.

¶ No published studies support a dose for this level of renal function.

# In patients with end-stage CKD on stable hemodialysis, prescribing information indicates the use of apixaban 5 mg BID with dose reduction to 2.5 mg BID if the patient is either  $\geq$ 80 years of age or body weight  $\leq$ 60 kg.

AF: atrial fibrillation; BID: twice daily; CKD: chronic kidney disease; Cr: creatinine; CrCl: creatinine clearance; INR: international normalized ratio; and QD: once daily.

Source: AHA/ACC/HRS 2014 Guideline for Management of AF.

### Warfarin alternatives

- Novel oral anticoagulants (dabigatran, rivaroxaban, and apixaban) have greater pharmacological predictability, fewer drug-to-drug interactions and dietary restrictions, and a lower risk of intracranial bleeding than warfarin.
- These new agents also have rapid onset and offset. Strict compliance is critical. If anticoagulation must be discontinued for a reason other than bleeding, consideration must be given to administering another antithrombotic (FDA boxed warning).
- There are no reliably effective reversal agents for warfarin alternatives. Agents such as prothrombin complex concentrate, activated prothrombin complex concentrate, or recombinant factor VIIa (rFVIIa) may be considered but have not been evaluated in clinical trials.

- Renal function should be assessed prior to prescribing a novel anticoagulant, as dosing for some agents must be adjusted for renal insufficiency. Renal function should be re-assessed when clinically indicated or at least annually.
  - Dabigatran, a direct thrombin inhibitor, is superior to warfarin for stroke prophylaxis in AF.<sup>3</sup>
  - Rivaroxaban, an oral factor Xa inhibitor, is noninferior to warfarin for the prevention of stroke or systemic embolism.<sup>4</sup>
  - Apixaban, an oral factor Xa inhibitor, is superior to warfarin in preventing stroke or systemic embolism, and is associated with less bleeding and lower mortality.<sup>5</sup>
  - Factor Xa inhibitors, edoxaban and bexiroxaban, are being evaluated by the FDA but are not approved for use in the US.

## Rate and Rhythm Control

- The AFFIRM, RACE, and AF-CHF trials have shown no mortality benefit to a rhythm control strategy compared to a rate control strategy.
- Therefore, a rate control strategy, without attempts at restoration or maintenance of sinus rhythm (SR), is reasonable in some patients with AF, especially those who are elderly and asymptomatic.
- If rate control offers inadequate symptomatic relief, restoration of SR may become a long-term goal and the patient should be referred to an electrophysiologist for rhythm control with drugs or ablation.

## Catheter Ablation for AF

- Catheter ablation is useful for patients with symptomatic paroxysmal AF who are refractory or intolerant to at least one class I or III antiarrhythmic drug (AAD) when the treatment strategy is rhythm control (Class I recommendation).
- Catheter ablation may be considered for patients with recurrent symptomatic paroxysmal AF prior to initiation/trial of an AAD after the comparative risks of drug and ablation are considered (Class IIa recommendation).
- Catheter ablation may be considered for patients with symptomatic persistent AF who are refractory or intolerant to at least one class I or class III AAD (Class IIa recommendation).
- The pulmonary veins (PVs) play a central role in triggering and/or maintaining the arrhythmic episodes in patients with AF. Electrical isolation of the PVs from the LA using catheter ablation eliminates AF in many patients.
- Catheter ablation for AF requires transseptal catheterization and has evolved from early attempts to target individual ectopic foci within the PV to circumferential electrical isolation of the entire PV musculature. Although there are many catheter ablation and surgical techniques available, electrical isolation of the PVs is a fundamental endpoint.
- Catheter ablation of the cavotricuspid isthmus should be considered first-line therapy for patients with typical atrial flutter and success rates are > 90%.

- The success rate of catheter ablation varies from 40-80% with one procedure. A repeat procedure can be effective in patients with recurrence.
- Patients with paroxysmal AF and minimal heart disease have better outcomes compared to patients with long-standing persistent AF and left atrial enlargement.
- The rate of major complications ranges from 2-12%. Complications include cardiac tamponade, vascular access complications, PV stenosis, stroke, atrio-esophageal fistula, phrenic nerve injury, catheter entrapment in the mitral valve, and left atrial flutter.
- The mortality rate is < 0.1%.
- Atrial tachyarrhythmias can occur in the first three months after ablation during the healing phase. These arrhythmias can be treated with medical therapy and often resolve. However, a repeat ablation procedure should be considered if atrial tachyarrhythmias persist.
- Patients should be anticoagulated for at least two months after ablation. Long-term oral anticoagulation should be considered in patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 2$  regardless of the outcome after ablation.
- The presence of left atrial thrombus is a contraindication to catheter ablation.

## Surgical Approaches

**Concomitant ablation:** AF ablation that achieves pulmonary vein isolation is reasonable for select patients undergoing cardiac surgery for another indication.

**Stand-alone ablation:** A stand-alone ablation procedure that achieves pulmonary vein isolation may be considered for highly symptomatic patients not well managed by other approaches.

## Ventricular Rate Control

### Principles of Rate Control Strategy

- Adequate control of the ventricular response during AF can significantly improve symptoms and is critical to avoid tachycardia-mediated cardiomyopathy.
- Most patients managed using a rhythm control strategy also require medications for rate control.
- Hospitalization is rarely required to control the ventricular response during AF, unless the patient is symptomatic.
- Rate control for atrial flutter tends to be more difficult than for AF.

### What is Adequate Rate Control?

- Control of the ventricular rate during AF is important both at rest and with exertion.
- Criteria for adequate rate control vary:
  - For the AFFIRM trial, adequate control was defined as an average HR < 80 bpm at rest and either an average rate < 100 bpm during Holter monitoring with no rate above 100% of the maximum age-adjusted predicted exercise HR, or a maximum HR of 110 bpm during a 6-min walk test.<sup>6</sup>
  - In the RACE II trial, lenient HR control (target < 110 bpm) was noninferior to strict HR control (resting rate < 80 bpm and rate during moderate exercise < 110 bpm).<sup>7</sup>

### Drugs to Control the Ventricular Response

AV nodal blocking drugs that can be used to control the ventricular response include:

#### **Beta blockers, Calcium channel antagonists (nondihydropyridine), and Digoxin**

- Beta blockers are the most effective drug class for rate control.
- Digoxin provides relatively poor rate control during exertion and should be reserved for patients who are sedentary or those with systolic HF.
- Digoxin does not convert AF to SR and may perpetuate AF.
- A combination of a beta blocker and either a calcium channel antagonist or digoxin may be needed to control the HR.
- The choice of medication should be individualized and the dose modulated to avoid bradycardia.
- Calcium channel antagonists should be avoided in HF patients.
- AV nodal blocking drugs at doses needed to control the ventricular response can cause symptomatic bradycardia requiring pacemaker therapy.

- Some antiarrhythmic drugs that are used to maintain sinus rhythm, such as sotalol, dronedarone, and amiodarone, also provide some control of the ventricular response when patients are in AF.
- Amiodarone should rarely be used for rate control only because of its potential for toxicity.
- IV digoxin or nondihydropyridine calcium channel antagonists are contraindicated in patients with ventricular preexcitation during AF (WPW syndrome) because they may accelerate the ventricular response and precipitate VF.
- Doses for commonly used drugs are shown on the back cover.

### AV Nodal Ablation

- Ablation of the AV conduction system and permanent pacing (the “ablate and pace” strategy) is an option for patients who have rapid ventricular rates despite maximum medical therapy and often yields remarkable symptomatic relief.
- There is growing concern about the negative effects of long-term RV pacing.
- Biventricular pacing may overcome many of the adverse hemodynamic effects associated with RV pacing and should be considered in patients with an LVEF of  $\leq 50\%$  undergoing AV nodal ablation.
- Catheter ablation of the AV node should only be considered after other rate-control strategies have been exhausted.

### Anticoagulation Considerations with Cardioversion

- For all patients with AF for > 48 hours, or when AF duration is unknown, 3 weeks of therapeutic anticoagulation is required prior to cardioversion (CV). Patients' self-reported symptoms can be an unreliable measure of AF duration due to AF that occurs during sleep or with minimal symptoms.
- Transesophageal echocardiography (TEE) to exclude the presence of LA thrombus can be used as an alternative to 3 weeks of anticoagulation prior to CV. For patients starting warfarin and at high risk for thromboembolism, heparin or low molecular weight heparin should be initiated and continued until a therapeutic level of warfarin has been established.
- Anticoagulation must be continued for at least 4 weeks after CV regardless of the use of TEE before CV. Anticoagulation after 4 weeks is dependent upon the patient's risk of stroke regardless of the perceived effectiveness of rhythm control.

## Restoration of Sinus Rhythm

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### Principles of Cardioversion

- CV may be achieved by means of a drug or an electrical shock.
- Direct-current CV is more effective than pharmacological CV.
- The more recent the onset of AF, the more effective is pharmacological CV.
- The primary disadvantage of electrical CV is that it requires sedation or anesthesia.
- The primary disadvantage of pharmacological CV is the risk of ventricular proarrhythmia.
- The risk of thromboembolism or stroke does not differ between pharmacological and electrical CV.
- Significant sinus bradycardia after CV can occur in patients on high-dose AV nodal blocking drugs.
- Antiarrhythmic drug therapy may be administered prior to CV to facilitate long-term success and maintenance of normal sinus rhythm.

### Direct Current Cardioversion

- Shocks should be delivered synchronous to the R-wave.
- The use of a biphasic defibrillator should be considered with 150-200 joules as the initial energy setting.
- When a rapid ventricular response does not respond promptly to pharmacological measures for AF patients with ongoing myocardial ischemia, symptomatic hypotension, angina, or HF, immediate CV is recommended.
- In case of early relapse of AF after CV, repeated direct-current CV attempts may be made following administration of antiarrhythmic medication.
- Electrical CV is contraindicated in patients with digitalis toxicity or hypokalemia.

### Pharmacological Cardioversion

- IV ibutilide is an effective drug available to convert AF.
  - Due to its risk of torsades de pointes, ibutilide should be avoided in patients with severe systolic dysfunction or a prolonged QTc (>480 ms).
  - More effective for conversion of atrial flutter than of AF; more effective in cases of more recent onset.
  - Can also be used to facilitate electrical CV when it is unsuccessful, or when there is an immediate recurrence of AF after initially successful CV.

- Consider IV magnesium (2 grams) prior to giving ibutilide to reduce risk of torsades de pointes.
- ECG monitoring must be performed for 4 hours after administration.
- Flecainide and Propafenone
  - Both flecainide and propafenone have been studied for their use as a “pill-in-the pocket” approach to cardioverting AF.
  - Generally, a beta blocker or a calcium channel blocker should be taken an hour prior to taking the antiarrhythmic drug when trying to convert AF to SR. For a person >70 Kg, 300 mg of flecainide or 600 mg of propafenone should be administered. For <70 Kg, the dose for flecainide and propafenone is 200 mg and 450 mg, respectively. After administration of the drug, heart rhythm must be monitored for at least 4-8 hours.

## Maintenance of Sinus Rhythm

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### Principles of Antiarrhythmic Drug Therapy

- Pharmacological therapy to maintain SR is indicated in patients who have troublesome symptoms related to paroxysmal AF or recurrent AF after CV who can tolerate antiarrhythmic drugs (AADs) and have a good chance of remaining in SR.
- AAD choice is based on side effect profiles and the presence or absence of structural heart disease, HF, and hypertension (see flow diagram).
- Drug choice should be individualized and must account for underlying renal and hepatic function.
- Goals of drug therapy are to decrease the frequency and duration of episodes, and to improve symptoms. AF recurrence while taking an AAD is not indicative of treatment failure and does not necessitate a change in antiarrhythmic therapy.
- An AAD should be abandoned when it does not result in symptomatic improvement or causes adverse effects.
- Ensure normal electrolyte status and appropriate anticoagulation prior to starting AAD therapy.
- Initiate AV nodal blockade prior to use of an AAD (e.g. flecainide) that does not provide substantial AV node blockade.
- Initiate therapy at low dose and titrate up as needed and after evaluating drug effects on ECG parameters.

## Specific Antiarrhythmic Drugs

### Flecainide/Propafenone

- Flecainide and propafenone are class IC drugs that delay conduction velocity by blocking sodium channels. Propafenone also exerts mild beta-blocking effects. These drugs have been shown to prolong the time to first recurrence of AF, but should not be used in patients with ischemic heart disease or LV dysfunction due to the high risk of proarrhythmia.
- Propafenone has significant first-pass hepatic metabolism, making dose titration important for therapeutic effect.
- These drugs can also be used for acute pharmacological conversion in a monitored setting.
- Class IC drugs can slow the atrial rhythm during AF resulting in acceleration of the ventricular response. Therefore, these agents should be combined with AV nodal blocking drugs to maintain rate control when AF recurs.
- Outpatient initiation may be considered in patients in sinus rhythm in the absence of structural heart disease or sinus or AV node dysfunction.

### Sotalol

- Sotalol is a nonselective beta-blocking drug with class III antiarrhythmic activity that prolongs repolarization. It is not effective for conversion of AF to sinus rhythm, but may be used to prevent AF. Sotalol should be avoided in patients with asthma, HF, renal insufficiency, or QT interval prolongation and should be used with caution in those at risk for torsades de pointes (e.g. female, age > 65 yr, renal dysfunction, taking diuretics).

### Dofetilide

- Dofetilide is a pure class III drug that prolongs repolarization by blocking the rapid component of the delayed rectified potassium current. Dofetilide was shown in the SAFIRE-D trial to be effective in maintaining sinus rhythm. To reduce the risk of early torsades de pointes, dofetilide must be initiated in the hospital at a dose titrated to renal function and the QT interval. Dofetilide is safe to use in patients with CAD or CHF. The FDA mandates prescriber registration and inpatient loading for initiation of this medication due to its proarrhythmic potential.

### Amiodarone

- Amiodarone is the most effective AAD, but is associated with relatively high toxicity, making it a second-line or last-resort agent in many cases.
- Amiodarone is an appropriate initial choice in patients with LVH, HF, or CAD, because it is associated with a low risk of proarrhythmia.
- Outpatient initiation may be considered in the absence of other risk factors for torsades de pointes and sinus or AV node dysfunction. Patients taking amiodarone should be monitored at least annually for thyroid, hepatic, and pulmonary toxicity.
- Low-dose amiodarone ( $\leq 200$  mg daily) is associated with fewer side effects than higher-dose regimens.

### Dronedarone

- Dronedarone is an analog of amiodarone with far lower risk of organ toxicity.
- Outpatient initiation may be considered in the absence of other risk factors for torsades de pointes and sinus or AV node dysfunction.
- Dronedarone is indicated to reduce the risk of cardiovascular hospitalization in patients with paroxysmal or persistent AF/AFL, with a recent episode of AF/AFL and associated cardiovascular risk factors, who are in sinus rhythm or who will be cardioverted.
- Dronedarone is contraindicated in patients with congestive heart failure. It is also contraindicated in patients with permanent AF (patients in whom sinus rhythm will not or cannot be restored) and for the sole purpose of rate control.
- There is a very small risk of liver toxicity with dronedarone and, therefore, liver function testing is recommended after drug initiation.

## DOSING GUIDELINE FOR DRUGS COMMONLY USED TO TREAT AF

DRUG	DOSING
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### HEART RATE CONTROL

Digoxin	IV: 0.25mg q2hrs (up to 1.5mg), then 0.125-0.375mg daily PO: 0.125-0.375mg daily
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#### Beta Blockers

Atenolol	PO: 25-100mg daily
Bisoprolol	PO: 2.5mg daily; can be titrated to 20mg daily
Carvedilol	PO: 3.125-25mg every 12 hrs (up to 50mg every 12 hrs for patients > 85kg), may use carvedilol sustained release 10-80mg daily
Esmolol	IV: 500 mcg/kg over 1 min, then 50-200 mcg/kg/min
Metoprolol	IV: 2.5-5mg bolus over 2 min (up to 3 doses) PO: 25-100mg bid, may use metoprolol succinate ER 25-200mg daily

#### Calcium Channel Blockers

Diltiazem	IV: 0.25mg/kg (avg 20mg) over 2 min (2 <sup>nd</sup> bolus can be given if HR >100bpm), then 5-15mg/hr PO: 120-360mg daily (slow release preferred)
Verapamil	IV: 0.075-0.15mg/kg over 2 min PO: 120-360mg daily (slow release preferred)

### HEART RHYTHM CONTROL

#### Vaughan Williams Class I

Flecainide	PO: 50-150mg every 12 hrs
Propafenone	PO: 150-300mg every 8 hrs, or sustained release 225-425mg every 12 hrs

#### Vaughan Williams Class III

Amiodarone	IV: 150mg over 10 min, then 0.5-1mg/min PO: 200mg TID x 2 weeks, 200mg BID x 2wks, then 200mg daily. Take with meals.
Dofetilide	PO: 125-500mcg every 12 hrs, based on renal function and QTc; must be initiated in the hospital
Dronedarone	PO: 400mg twice daily with meals
Ibutilide	IV: ≥ 60kg – 1 mg over 10 min; <60kg – 0.01mg/kg over 10 min, while observing for QTc prolongation and ventricular proarrhythmia. Dose can be repeated after 10 min but the risk of proarrhythmia increases. Pretreatment with MgSO <sub>4</sub> 1-2gm IV may reduce the risk of TdEP.
Sotalol	PO: 80mg BID, to a maximum of 240-320mg/day, based on renal function and QTc

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