

Heart Rhythm SocietySM
Restoring the Rhythm of Life

AF 360°

Practical Rate and Rhythm Management of Atrial Fibrillation

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Adapted from the ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation

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Editor: Bradley P. Knight, MD, FHRS
Assistant Editors: Matthew Sorrentino, MD,
M. Craig Delaughter, MD, Ph.D., Dipak P. Shah, MD

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GENERAL APPROACH TO THE PATIENT WITH AF

1. Establish an Accurate Diagnosis of AF

- AF is characterized by replacement of consistent P waves with fibrillatory waves, varying in amplitude, shape, and timing.
- The ventricular response is chaotic and frequently rapid when atrioventricular conduction is intact.
- In patients with pacemakers, diagnosis of AF may require temporary inhibition of the pacemaker to expose AF activity.
- AF should be distinguished from atrial flutter, which has regular organized atrial activity with a rate typically between 240 and 320 bpm, multifocal atrial tachycardia, which has a single P wave from multiple atrial foci preceding each QRS, and regular supraventricular tachycardias such as AV nodal reentry.

2. Determine Symptoms, Clinical History, and AF Pattern

- Clinical type of AF can be classified as:
 - Paroxysmal (≤ 7 days), which is self-terminating
 - Persistent (> 7 days), which requires intervention for termination
 - Permanent, which is refractory to cardioversion (CV) or accepted as a final rhythm
- Onset of the first symptomatic attack or date of discovery of AF
- The onset of the current episode, if persistent
- Presence and nature 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
- An event recorder can be useful when trying to correlate symptoms with rhythm.

3. Exclude 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 individualize AF management.
- Coronary artery disease should be excluded in patients with risk factors but is rarely a reversible cause of AF.

4. Identify Correctable Secondary Causes

- Rule out potentially correctable causes such as sleep apnea, hyperthyroidism, WPW, and drug or alcohol use.

5. Develop a Treatment Strategy

Management Principles

- A comprehensive treatment plan must address the three cornerstones of AF management: (1) rate control, (2) rhythm control, and (3) prevention of thromboembolism.
- Goals of therapy include symptom control, stroke prevention, and a reduction in hospitalizations.
- Hospitalization should be considered in patients who are significantly symptomatic, hemodynamically unstable, or before initiation of antiarrhythmic drug therapy.
- Electrical CV 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 who continue to be symptomatic or are difficult to manage should be referred to an electrophysiologist.

GENERAL APPROACH (CONTINUED)

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.
- Restoration and maintenance of sinus rhythm continues to be a reasonable treatment approach in many patients with AF.

Stroke Prevention

- Antithrombotic therapy to prevent thromboembolism is recommended for all patients with AF regardless of whether a rhythm or rate control strategy is chosen, except those with lone AF or contraindications to warfarin therapy.
- Aspirin plus clopidogrel is not a substitute for warfarin. However, in the ACTIVE-A trial, aspirin combined with clopidogrel was more effective than aspirin alone in preventing strokes in high-risk patients who were not suitable for warfarin therapy, but caused more major bleeding than aspirin alone.
- Antithrombotic therapy is recommended for patients with atrial flutter as for those with AF.
- In patients with AF who do not have mechanical valves, it is reasonable to interrupt anticoagulation for up to 1 week without substituting heparin for procedures that carry a risk of bleeding.
- Alternatives to warfarin, including factor Xa and direct thrombin inhibitors, are being investigated.
- Patients with AF who have hypertrophic cardiomyopathy, mitral stenosis, or a mechanical valve should be treated with warfarin.
- The CHADS₂ scoring system can be used to risk stratify patients with nonvalvular AF to determine the need for warfarin. The annual risk of stroke with a CHADS₂ score of 0 is 1.9%, but the annual risk of stroke with a CHADS₂ score of 6 is 18.2%.

CHADS ₂ Risk Criteria	Score	CHADS ₂ Score	Recommended Therapy
Congestive Heart Failure	1	0	Aspirin (81 to 325 mg daily) *
Hypertension	1	1	Aspirin (81 to 325 mg daily) or Warfarin (INR 2.0 to 3.0, target 2.5)**
Age ≥ 75 Years	1	≥ 2	Warfarin (INR 2.0 to 3.0, target 2.5)**
Diabetes Mellitus	1		
Stroke or TIA in the past	2		

* Aspirin or no therapy is acceptable for patients of age less than 60 y, and with no heart disease (lone AF).

** If mechanical valve, target international normalized ratio (INR) greater than 2.5.

Anticoagulation Considerations with Cardioversion

- For all patients with AF for > 48 hours, or when AF duration is unknown, 3 weeks of therapeutic anticoagulation with an INR ≥ 2.0 is required prior to CV.
- TEE can be used to assess the LA for thrombus as an alternative to 3 weeks of anticoagulation, but patients must still be therapeutically anticoagulated with warfarin or heparin at the time of CV.
- 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 CHADS₂ score.

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.
- Rate control during atrial flutter tends to be more difficult than during AF.

What is Adequate Rate Control?

- Control of the ventricular rate during AF is important both at rest and with exertion.
- No standard method for assessment of heart rate (HR) control has been established.
- Criteria for rate control vary with patient age but usually involve achieving ventricular rates between 60 and 80 bpm at rest and between 90 and 115 bpm during moderate exercise.

RESTORATION OF SINUS RHYTHM

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 torsades de pointes.
- The risk of thromboembolism or stroke does not differ between pharmacological and electrical CV.
- Be prepared for significant sinus bradycardia after CV in patients on high-dose AV nodal blocking drugs.

Direct Current Cardioversion

- Shocks should be delivered synchronous to the R-wave.
- The use of a biphasic defibrillator should be considered.
- When a rapid ventricular response does not respond promptly to pharmacological measures for patients with AF 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.
 - Alternative to electrical CV for patients who do not have very low ejection fractions or a prolonged QTc interval.
 - 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.
 - Electrocardiographic (ECG) monitoring must be performed for 4 hours after administration.

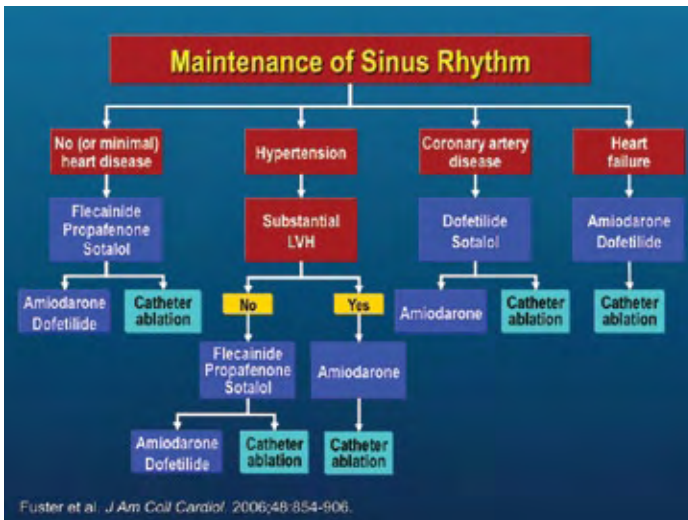
- For the AFFIRM trial, adequate control was defined as an average HR up to 80 bpm at rest and either an average rate up to 100 bpm during Holter monitoring with no rate above 100% of the maximum age-adjusted predicted exercise HR, or a maximum HR of 110 bpm during a 6-min walk test.
- In the RACE trial, rate control was defined as less than 100 bpm at rest. Only about 5% of patients from these trials required AV ablation to achieve HR control.

Drugs to Control the Ventricular Response

- AV nodal blocking drugs that can be used to control the ventricular response include:
 - Beta blockers — Calcium channel antagonist (nondihydropyridine) — 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 with systolic HF.

MAINTENANCE OF SINUS RHYTHM

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 and have a good chance of remaining in SR.
- Antiarrhythmic drug 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.
- Drugs should be used to decrease the frequency and duration of episodes, and to improve symptoms. AF recurrence while taking an antiarrhythmic drug is not indicative of treatment failure and does not necessitate a change in antiarrhythmic therapy.
- An antiarrhythmic drug should be abandoned when it does not result in symptomatic improvement or causes adverse effects.
- Ensure normal electrolyte status and appropriate anticoagulation per CHADS₂ score prior to starting antiarrhythmic drug therapy.
- Initiate AV nodal blockade prior to use of antiarrhythmics (e.g., flecainide) that do not provide substantial AV node blockade.
- Initiate therapy at low dose and titrate up as needed and after evaluating drug effects on ECG parameters.

- 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.
- Beta blockers and calcium channel antagonists should be used cautiously in patients with HF.
- AV nodal blocking drugs at doses required to control the ventricular response can cause symptomatic bradycardia that requires 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 because of its potential for toxicity.

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.
- Class IC drugs can slow the atrial rhythm during AF resulting in acceleration of the ventricular response. Therefore, additional AV nodal blocking drugs are generally required to maintain rate control when AF recurs.

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.

Dofetilide

- Dofetilide is a pure class III drug that prolongs repolarization by blocking the rapid component of the delayed rectifier 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.

Amiodarone

- Amiodarone is the most effective antiarrhythmic drug, 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.
- Patients taking amiodarone should be monitored regularly for thyroid, hepatic, and pulmonary toxicity.
- Low-dose amiodarone (≤ 200 mg daily) is associated with fewer side effects than higher-dose regimens.

Dronedarone*

- Dronedarone is an analog of amiodarone without the risk of organ toxicity.
- 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 NYHA Class IV heart failure or NYHA Class II-III heart failure with a recent decompensation requiring hospitalization or referral to a specialized heart failure clinic.

* Dronedarone is a newly approved therapy and is not included in the current guidelines. See FDA approved labeling indications.

- IV digoxin or nondihydropyridine calcium channel antagonists given to patients with AF and WPW may accelerate the ventricular response and are not recommended.
- Doses for commonly used drugs are on reverse side.

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, on the other hand, may overcome many of the adverse hemodynamic effects associated with RV pacing.
- Catheter ablation of the AV node should not be attempted without a prior trial of medication to control the rate.

CATHETER ABLATION FOR AF

- The pulmonary veins (PVs) are an important source of triggered activity and reentry in patients with AF.
- Electrical isolation of the PVs from the LA using catheter ablation eliminates AF in some 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 has been proven to be effective and is currently considered a second-line therapy in patients with AF who continue to be highly symptomatic despite a trial of one or more antiarrhythmic drugs.
- In some patients, especially young individuals with very symptomatic AF, ablation may be preferred over years of drug therapy.
- The success rate of catheter ablation varies from 40-90% 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 range from 2-12%. Complications include cardiac tamponade, vascular access complications, PV stenosis, stroke, left atrial 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 within the first two 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 with warfarin for at least two months after ablation. Long-term oral anticoagulation should be considered in patients with a CHADS2 score > 1 regardless of the outcome after ablation. A left atrial thrombus is a contraindication to catheter ablation.
- Catheter ablation of the cavotricuspid isthmus should be considered first line therapy for patients with typical atrial flutter.

DOSING GUIDELINE FOR DRUGS COMMONLY USED TO TREAT AF

DRUG	HRS IV LOADING DOSE & IV MAINTENANCE DOSE
Heart Rate Control	
Esmolol	IV: 500 mcg/kg, 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
Atenolol	PO: 25-100mg 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
Verapamil	IV: 0.075-0.15mg/kg over 2 min PO: 120-480mg daily (slow release available and preferred)
Diltiazem	IV: 0.25 mg/kg (avg. 20mg) over 2 min (2nd bolus can be given if HR >100 bpm), then 5-15mg/hr PO: 120-480mg daily (slow release available and preferred)
Digoxin	IV: 0.25 mg q2hrs (up to 1.5mg), then 0.125-0.375mg daily PO: 0.125-0.375mg daily
Heart Rhythm Control	
Vaughan Williams Class I	
Flecainide	PO: 50-150 mg every 12 hrs
Propafenone	PO: 150-300 mg every 8 hrs, or sustained release (SR) 225-425 mg every 12 hrs
Vaughan Williams Class III	
Ibutilide	IV: 1mg over 10 minutes, while observing for QTc prolongation and ventricular proarrhythmia. Dose can be repeated after 10 minutes, but the risk of proarrhythmia increases.
Sotalol	PO: 80-160mg, to a maximum of 320mg every 12 hours, based on renal function
Dofetilide	PO: 125-500mcg every 12 hours, based on renal function; must be initiated in the hospital
Amiodarone	IV: 150mg over 10 min, then 0.5-1mg/min PO: 800mg daily for 1 wk, 600mg daily for 1 wk, 400mg daily for 4-6 wks, then 200mg daily
Dronedarone	PO: 400mg twice daily, with meals



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