Treatment Guidelines
from The Medical Letter®

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Tables

Treatment of Atrial Fibrillation

The treatment of atrial fibrillation includes ventricular rate control, anticoagulation, conversion to normal sinus rhythm and maintenance of sinus rhythm. The choice of therapies that can achieve these goals is discussed in the text that follows. Some drugs are recommended here for indications that have not been approved by the FDA.

RATE CONTROL

In recent years, controlled trials have shown that slowing of the ventricular rate during atrial fibrillation is as effective as rhythm control with cardioversion and/or antiarrhythmic drugs (which can be proarrhythmic) in preventing serious complications and death.[1]

Table 1. Some Rate Control Agents: Dosage and Adverse Effects

Drug	Some Oral Formulations	Usual Adult Dosage[1]	Adverse Effects
Beta-Adrenergic Blockers			
Esmolol *(Brevibloc*, and others*)*	—	IV loading: 500 mcg/kg over 1 min, followed by 50 mcg/kg/min for 4 min; titrate to desired effect IV maintenance: 60-200 mcg/kg/min	Heart block, hypotension, heart failure, bradycardia, bronchospasm, pain at infusion site
Metoprolol *(Lopressor*, *Toprol XL*, and others*)*	50 or 100 mg tabs; 25, 50, 100 200 mg ER tabs	PO: 50-200 mg/d divided q12-24h[2] IV: 2.5-5 mg over 2 min (up to 3 doses)	Heart block, hypotension, heart failure, bradycardia, bronchospasm, depression
Propranolol *(Inderal*, *Inderal LA*, and others*)*	10, 20, 40, 60, 80 mg tabs; 60, 80, 120, 160 mg ER caps	PO: 80-240 mg/d divided q6-24h[2] IV: 0.15 mg/kg (1 mg/min)	Heart block, hypotension, heart failure, bradycardia, bronchospasm, depression
Calcium Channel Blockers			
Diltiazem *(Cardizem*, *Cardizem LA*, and others**)**	30, 60, 90, 120 mg tabs; 120, 180, 240, 300, 360, 420 mg ER caps	PO: 120-360 mg/d divided q6-24h[2] IV loading: 0.25 mg/kg over 2 min, may be repeated in 15 min IV maintenance: 5-15 mg/hr	Heart block, hypotension, heart failure, aystole
Verapamil *(Calan*, *Isoptin SR*, and others*)*	40, 80, 120 mg tabs; 120, 180, 240 mg ER tabs or caps	PO: 120-360 mg/d divided q6-24h[2] IV loading: 0.075-0.15 mg/kg over 2 min (max 20 mg)	Heart block, hypotension, heart failure, asystole, dizziness, headache, fatigue, edema, nausea, constipation
Digoxin			
Digoxin *(Lanoxin,* and others*)*	0.125 or 0.25 mg tabs	PO loading: 0.75-1.5 mg in 3-4 divided doses over 24 hrs PO and IV maintenance: 0.125-0.375 mg/d IV loading: 0.5-1 mg in 3-4 divided doses over 24 hrs	Bradycardia, AV block, arrhythmias, anorexia, nausea, vomiting, diarrhea, abdominal pain, headache, confusion, abnormal vision

ER = Extended-release formulation
1. Patients with decreased hepatic or renal function may require lower dosage.
2. Dosage given as a range; dose and interval will vary depending on formulation used.

Therefore, ventricular rate control is now often used as first-line therapy for management of chronic atrial fibrillation, unless symptoms persist.[2] Lenient rate control (<110 beats per minute), particularly in patients with a structurally normal heart and no heart failure, may be as effective as strict rate control (<80 beats per minute) in preventing stroke and death.[3] The drugs most commonly used for rate control in atrial fibrillation are beta-blockers, the non-dihydropyridine calcium channel blockers and digoxin.

BETA-ADRENERGIC BLOCKERS — A beta-blocker such as propranolol or metoprolol can control the ventricular rate in atrial fibrillation or flutter. Esmolol is an IV cardio-selective beta-blocker with an elimination half-life of about 9 minutes that is effective for short-term use in controlling the ventricular response in atrial flutter or fibrillation, particularly after cardiac surgery; both therapeutic and adverse effects (hypotension, bradycardia) usually disappear within 30 minutes after stopping the infusion. Beta-blockers should be used cautiously in patients with heart failure.

CALCIUM CHANNEL BLOCKERS — Verapamil and diltiazem prolong AV nodal refractoriness and are effective in slowing the ventricular rate in atrial fibrillation or flutter. Their IV use can be complicated by hypotension or bradycardia, especially with concurrent use of other cardiodepressant drugs in patients with underlying heart disease. Verapamil and diltiazem may accelerate ventricular response during atrial fibrillation in patients with bypass tracts and are therefore contraindicated in patients with Wolff-Parkinson-White syndrome. Usual doses of dihydropyridine calcium channel blockers (all the other calcium channel blockers available in the US) generally have no rate-controlling activity. Verapamil and diltiazem may be preferred over beta-blockers for long-term use in patients with chronic obstructive pulmonary disease (COPD). As with beta-blockers, they should be used cautiously in patients with heart failure.

DIGOXIN — Digoxin, generally used as an adjunctive agent, can help control ventricular response in atrial fibrillation or flutter, but other drugs are more effective. It may be an initial choice in patients with systolic heart failure. Digoxin, like verapamil and diltiazem, should not be used in patients with Wolff-Parkinson-White syndrome.

ANTICOAGULATION

Atrial fibrillation increases the risk of thromboembolic stroke by a factor of 4 to 5.[4] Anticoagulation can reduce the risk of thromboembolic stroke in patients with atrial fibrillation by 60% or more and has been shown to be more effective than antiplatelet therapy for this indication.

WARFARIN — In patients with atrial fibrillation who have had a previous stroke, transient ischemic attack or non-CNS embolus, or have two or more other risk factors for stroke (>75 years old; hypertension; diabetes; heart failure), the benefits of long-term warfarin therapy in preventing ischemic stroke far surpass the risk of major bleeding. In those with no history of stroke, TIA or non-CNS embolus, and only one additional risk factor ($CHADS_2$ score = 1), either warfarin or aspirin could be used. In patients with atrial fibrillation who are ≤75 years old and have no risk factors ($CHADS_2$ score = 0), aspirin is the drug of choice.[5]

Table 2. $CHADS_2$ Scoring

	Condition	Points
C	Heart Failure	1
H	Hypertension	1
A	Age >75 years	1
D	Diabetes Mellitus	1
S_2	Prior Stroke or TIA	2

Dosing – The main drawback of warfarin has been the need for close monitoring to keep the international normalized ratio (INR) between 2 and 3. Traditionally, warfarin has been dosed empirically. The usual starting dosage range is 2-5 mg once daily, varying with the weight and age of the patient. By adjusting the dose based on the INR, clinicians eventually arrive at the therapeutic dose. Algorithms that include multiple clinical predictors of warfarin dosing are available at www.warfarindosing.org.

Genetic variations in the C1 subunit of vitamin K epoxide reductase (VKORC1) and the hepatic enzyme CYP2C9 account for 30-35% of the variability in the therapeutic dose of warfarin. When factors such as age and body size are included, they account for about 50%.[6] Genotyping patients for these single nucleotide polymorphisms (SNPs) may help in estimating the therapeutic dose. A prospective study in 896 patients starting warfarin therapy showed that warfarin genotyping reduced the risk of hospitalization for bleeding and thromboembolism.[7] Tests for these SNPs are now available from commercial laboratories.

Drug Interactions – Maintaining the INR in the desired range is made more difficult by warfarin's numerous interactions with other drugs.[8] Some of these are listed in Table 3. In patients with atrial fib-

Table 3. Some Drug Interactions with Warfarin

Increased Anticoagulant Effect	Decreased Anticoagulant Effect
Acetaminophen *(Tylenol*)*	Barbiturates
Amiodarone *(Cordarone*)*	Carbamazepine *(Tegretol*)*
Cefazolin *(Kefzol*)*	Cholestyramine *(Questran*)*
Cefotetan	Colestipol *(Colestid*)*
Ceftriaxone *(Rocephin*)*	Dicloxacillin
Clarithromycin *(Biaxin*)*	Nafcillin
Erythromycin *(Ery-Tab*)*	Phenytoin (*Dilantin**)
Fluoroquinolones	Rifampin *(Rifadin*)*
Fluorouracil	St. John's Wort
Fluconazole *(Diflucan*)*	Sucralfate *(Carafate*)*
Fluoxetine *(Prozac*)*	
Fluvastatin *(Lescol)*	
Fluvoxamine *(Luvox*)*	
Metronidazole *(Flagyl*)*	
Phenytoin *(*initial; *Dilantin*)*	
Rosuvastatin *(Crestor)*	
Trimethoprim-sulfamethoxazole *(Bactrim*)*	
Voriconazole *(Vfend*)*	

*And others.

rillation, the most important of these is with amiodarone, which decreases the warfarin dose requirement by a third to a half. Another common interaction is with the widely used analgesic acetaminophen. Occasional use of acetaminophen generally has little or no effect on the INR in patients on chronic warfarin therapy, but in some patients even a few grams of acetaminophen can cause a dramatic increase in INR. Patients on chronic warfarin therapy who take more than 2 g per day of acetaminophen for more than a few days should be monitored closely for INR changes.

AN ORAL DIRECT THROMBIN INHIBITOR — Direct thrombin inhibitors can also prevent thromboembolic stroke in patients with atrial fibrillation, and they do not require monitoring or frequent dose adjustments, but all those currently available in the US must be given parenterally.[9] Dabigatran etexilate, an oral direct thrombin inhibitor, is investigational in the US, but is available in Canada (*Pradax* – Boehringer Ingelheim) and in Europe *(Pradaxa)*.

A Clinical Trial – In the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY), 18,113 patients (mean age 71 years) with atrial fibrillation considered at risk for stroke received dabigatran 110 or 150 mg twice daily (blinded) or adjusted-dose warfarin (unblinded) to achieve an INR between 2 and 3 and were followed for a median of 2 years for the primary endpoint of stroke or systemic embolism. About 20% of the participants were on concomitant aspirin therapy. The rates per year of the primary endpoint were 1.69% with warfarin, 1.53% with dabigatran 110 mg and 1.11% with dabigatran 150 mg. The rate of stroke and systemic embolism with the higher dose of dabigatran was significantly lower than the rate with warfarin.[10]

Adverse Effects – The rate of major bleeding in the RE-LY trial was 3.36% with warfarin, 2.71% with dabigatran 110 mg (a statistically significant difference) and 3.11% with dabigatran 150 mg. The rate of hemorrhagic stroke was significantly lower with both doses of dabigatran than with warfarin. Both doses of dabigatran were associated with a slightly higher risk of myocardial infarction: 0.53% with warfarin; 0.72% with dabigatran 110 mg; and 0.74% with dabigatran 150 mg.[10]

ORAL FACTOR Xa INHIBITORS — Although not yet approved for use in the US, several oral factor Xa inhibitors are in clinical trials for use in atrial fibrillation. Like direct thrombin inhibitors, these agents offer anticoagulation without the need for monitoring. One oral factor Xa inhibitor, rivaroxaban (*Xarelto* – Bayer), is available in Canada.[11]

RHYTHM CONTROL

The treatment of choice for urgent conversion of atrial fibrillation to normal sinus rhythm is DC cardioversion. Antiarrhythmic drugs and catheter ablation are used to maintain normal sinus rhythm. All of these rhythm control options are generally reserved for symptomatic patients.

DRUG THERAPY — The antiarrhythmic drugs most commonly used now to prevent episodes of paroxysmal atrial fibrillation and to maintain sinus rhythm after cardioversion are listed in Table 4. The choice of a specific agent varies with the clinical status of the patient and the preferences of the clinician. Guidelines for the choice of agents are available from the American College of Cardiology and the American Heart Association.[1]

Propafenone and **flecainide** are generally reserved for patients with structurally normal hearts. **Sotalol**, a non-selective beta-blocker, is better tolerated than quinidine or some other older drugs now seldom used for this indication, but it increases the QT interval and should be avoided in patients with baseline QT prolongation or in those receiving other drugs that also prolong the QT interval (see Table 5). **Disopyramide** is sometimes used to maintain normal sinus rhythm in patients with vagally-induced atrial fibrillation. **Dofetilide** has been effective in patients with compromised left ventricular function.

Table 4. Some Rhythm Control Agents: Dosage and Adverse Effects[1]

Drug	Some Oral Formulations	Usual Adult Dosage[2]	Adverse Effects[3]
Amiodarone			
(*Cordarone*, and others)	100, 200, 300 or 400 mg tabs	PO loading: 800 mg/d in 2 doses to a total of 10 g PO maintenance: 100-400 mg/d IV loading: 150 mg over 10 min, which can be repeated once, followed by 360 mg over 6 hrs (not to exceed 2100 mg/24 hrs) IV maintenance: 0.5-1 mg/min Cardiac arrest: 300 mg IV push	PO: Pulmonary fibrosis, bradycardia, heart block, QT prolongation and possible torsades de pointes (unusual), hyper- or hypothyroidism, GI upset, alcoholic-like hepatitis, peripheral neuropathy, ataxia, tremor, dizziness, photosensitivity, blue-gray skin, corneal microdeposits, optic neuritis IV: Hypotension, bradycardia, phlebitis at site of administration, torsades de pointes
Disopyramide			
(*Norpace*, *Norpace CR*, and others)	100 or 150 mg caps; 100 or 150 mg ER caps	PO: 400-750 mg/d divided q6-12h[4]	Anticholinergic effects (urinary retention, aggravation of glaucoma, constipation) hypotension, heart failure, ventricular tachyarrhythmias, QT prolongation, possible torsades de pointes, heart block, nausea, vomiting, diarrhea, hypoglycemia, nervousness
Dofetilide[5]			
(*Tikosyn*)	0.125, 0.25 or 0.5 mg caps	PO: 0.125-0.5 mg bid	Torsades de pointes
Dronedarone			
(*Multaq*)	400 mg tabs	PO: 400 mg bid	Diarrhea, nausea, vomiting, abdominal pain, photosensitivity, QT prolongation
Flecainide[6]			
(*Tambocor*, and others)	50, 100 or 150 mg tabs	PO initial: 50-100 mg q12h, may increase q4 days by 50 mg q12h if required; usual max 400 mg/d PO maintenance: ≤400 mg/d	Bradycardia, heart block, new ventricular fibrillation, sustained ventricular tachycardia, heart failure, dizziness, blurred vision, nervousness, headache, GI upset, neutropenia
Propafenone[6]			
(*Rythmol*, *Rythmol SR*, and others)	150, 225 or 300 mg tabs; 225, 325 or 425 mg ER caps	PO initial: 450 mg/d divided q8-12h,[4] increase q3-5 days if required; max 850-900 mg/d PO maintenance: 225-425 mg (ER) q12h	Bradycardia, heart block, new ventricular fibrillation, sustained ventricular tachycardia, heart failure, dizziness, lightheadedness, metallic taste, GI upset, bronchospasm, hepatic toxicity
Sotalol[6]			
(*Betapace*, *Betapace AF*, and others)	80, 120, 160 or 240 mg tabs[8]	PO: 80-160 mg bid	Heart block, hypotension, bronchospasm, bradycardia; higher doses are associated with increased adverse effects including QT prolongation and possible torsades de pointes

ER = Extended-release formulation
1. All of these drugs require monitoring at initiation for proarrhythmias.
2. Patients with decreased hepatic or renal function may require lower dosage.
3. Rhythm control agents and some other drugs that prolong the QT interval are listed in Table 5.
4. Dosage given as a range; dose and interval will vary depending on formulation used.
5. Available through a restricted distribution program.
6. Should not be used in patients with heart failure or ischemic heart disease.
7. *Betapace AF* is not available in 240-mg tablets.

Amiodarone is the most effective antiarrhythmic for maintenance of sinus rhythm, but it can cause multiple adverse effects, some severe, and has many interactions with other drugs (see Table 6). **Dronedarone**, a non-iodinated analog of amiodarone, may prove to be safer than amiodarone, but in clinical trials it has been less effective, and one clinical trial in patients with new or worsening heart failure was terminated prematurely because of a significant increase in mortality in dronedarone-treated patients.[12,13]

CATHETER ABLATION — Radiofrequency ablation is the cauterization of cardiac tissue responsible for triggering or maintaining an arrhythmia. In recent years, some controlled trials with short-term follow-up have found catheter ablation superior to antiarrhythmic

Table 5. Some Drugs That May Prolong the QTc Interval*

Amiodarone *(Cordarone,* and others*)*	Haloperidol *(Haldol,* and others*)*
Chloroquine *(Aralen,* and others*)*	Ibutilide *(Corvert,* and others*)*
Chlorpromazine *(Thorazine,* and others*)*	Methadone *(Dolophine,* and others*)*
Clarithromycin *(Biaxin,* and others*)*	Pentamidine *(Pentam,* and others*)*
Disopyramide *(Norpace,* and others*)*	Pimozide *(Orap)*
Dofetilide *(Tikosyn)*	Procainamide
Dronedarone *(Multaq)*	Quinidine
Droperidol *(Inapsine)*	Sotalol *(Betapace,* and others*)*
Erythromycin *(Ery-Tab,* and others*)*	Thioridazine

*All have been associated with torsades de pointes. Adapted from www.azcert.org.

drugs in maintaining sinus rhythm and improving symptoms, exercise capacity and quality of life.[14-16]

AV Node Ablation – For many years, the only catheter ablation technique applicable to patients with atrial fibrillation was atrioventricular (AV) node ablation, which can relieve symptoms and improve functional capacity, but creates the need for a permanent pacemaker and leaves the patient with a continuing need for anticoagulation because the atria continue to fibrillate.

Pulmonary Vein Isolation – Recognition that pulmonary veins are often the source of ectopic beats that trigger paroxysmal atrial fibrillation led to catheter ablation of foci within them. The occasional development of pulmonary vein stenosis, a serious complication, led to current techniques in which multiple ablation lesions are placed to electronically isolate the veins from the left atrium. A prospective controlled trial in patients with symptomatic, drug-resistant atrial fibrillation, an ejection fraction of ≤40% and NYHA class II or III heart failure found pulmonary vein isolation superior to AV node ablation.[17]

The long-term success of pulmonary vein isolation, usually defined as freedom from symptomatic arrhythmia (on or off antiarrhythmic drugs) months after the procedure, is generally 50-80%. It is most likely to be effective when atrial fibrillation is paroxysmal.

The most common complication of pulmonary vein isolation has been left atrial flutter, which usually occurs in the first few weeks after ablation and may resolve within 3-4 months; highly symptomatic patients may need a second procedure to ablate left atrial flutter. Uncommon but serious complications have included atrial perforation, cardiac tamponade, thromboembolism and atrio-esophageal fistula.

Postablation Care – Patients usually are hospitalized overnight and treated with a heparin infusion. On discharge, anticoagulation with warfarin is continued for at least 2-3 months. To minimize symptoms from early recurrences of atrial fibrillation/flutter, antiarrhythmic drug therapy is often added for about the same period of time.

Table 6. Some Cardiovascular Drug Interactions with Amiodarone

Interacting Drug	Effects
Amlodipine *(Norvasc,* and others*)*	Possible increased serum concentrations of amlodipine
Atorvastatin *(Lipitor)*	Possible increased risk of myopathy and rhabdomyolysis
Beta-adrenergic blockers	Possible increased beta-blocker effect
Digoxin *(Lanoxin,* and others*)*	Possible digoxin toxicity
Diltiazem *(Cardizem,* and others*)*	Possible increased serum concentrations of amiodarone and/or diltiazem
Felodipine *(Plendil,* and others*)*	Possible increased serum concentrations of felodipine
Ibutilide *(Corvert,* and others*)*	Possible QT interval prolongation
Isradipine	Possible increased serum concentrations of isradipine; possible QT interval prolongation
Lovastatin *(Mevacor,* and others*)*	Possible increased risk of myopathy and rhabdomyolysis
Nicardipine *(Cardene, Cardene SR)*	Possible increased serum concentrations of nicardipine; possible QT interval prolongation
Nifedipine *(Procardia,* and others*)*	Possible increased serum concentrations of nifedipine
Nimodipine	Possible increased serum concentrations of nimodipine
Nisoldipine *(Sular)*	Possible increased serum concentrations of nisoldipine
Simvastatin *(Zocor,* and others*)*	Possible increased risk of myopathy and rhabdomyolysis
Sotalol *(Betapace,* and others*)*	Possible QT interval prolongation and possible increased risk of bradycardia and sinus arrest
Verapamil *(Calan,* and others*)*	Possible increased serum concentrations of amiodarone and/or verapamil
Warfarin *(Coumadin,* and others*)*	Increased serum concentrations of warfarin

CONCLUSION

The first priority in treatment of atrial fibrillation is rate control. Lenient rate control (<110 beats/minute) appears to be as beneficial as strict control (<80 beats/minute) in some patients. The drugs most commonly used for rate control are beta-blockers, verapamil, diltiazem and digoxin.

The next priority is thromboembolic risk reduction. In patients with additional risk factors for stroke, warfarin is more effective than aspirin. For patients with a low risk of stroke, aspirin would be a reasonable choice. Emerging agents such as direct thrombin inhibitors and oral Xa inhibitors may offer predictable anticoagulant effects without the need for monitoring.

Rhythm control is important mainly for persistently symptomatic patients. Antiarrhythmic drugs, electrical cardioversion and radiofrequency ablation are options for such patients.

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Through this program, The Medical Letter expects to provide the health care community with educational content that they will use to make independent and informed therapeutic choices in their practice.

LEARNING OBJECTIVES:
The objective of this program is to meet the need of health care professionals for unbiased, reliable and timely information on treatment of major diseases. Participants will be able to select and prescribe, or confirm the appropriateness of the prescribed usage of, the drugs and other therapeutic modalities discussed in Treatment Guidelines with specific attention to clinical evidence of effectiveness, adverse effects and patient management.

Upon completion of this program, the participant will be able to:

1. Explain the current approach to the management of a patient with atrial fibrillation including rate control, rhythm control and anticoagulation
2. Identify which patients may be candidates for more aggressive management strategies such as antiarrhythmic drugs or catheter ablation
3. Discuss the pharmacologic options available for rate and rhythm control in patients with atrial fibrillation and compare them based on their efficacy, dosage and administration, potential adverse effects and drug interactions
4. Review the drugs available for prevention of thromboembolism in patients with atrial fibrillation and recognize which patients might benefit from long-term warfarin therapy
5. Determine the most appropriate therapy given the clinical presentation of an individual patient with atrial fibrillation

Privacy and Confidentiality: The Medical Letter guarantees our firm commitment to your privacy. We do not sell any of your information. Secure server software (SSL) is used for commerce transactions through VeriSign, Inc. No credit card information is stored.

IT Requirements: Windows 98/NT/2000/XP/Vista/7, Pentium+ processor, Mac OS X+ w/ compatible process; Microsoft IE 6.0+, Mozilla Firefox 2.0+ or any other compatible Web browser. Dial-up/high-speed connection.

Have any questions? Call us at 800-211-2769 or 914-235-0500 or e-mail us at: custserv@medicalletter.org

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Issue 97 Questions

1. The method now often used as first-line therapy for management of chronic atrial fibrillation is:
   a. ventricular rate control
   b. rhythm control with antiarrhythmic drugs
   c. rhythm control with cardioversion
   d. all of the above

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2. The drugs most commonly used for rate control in patients with atrial fibrillation include:
   a. beta-blockers
   b. non-dihydropyridine calcium channel blockers
   c. digoxin
   d. all of the above

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3. A 64-year-old female with a history of diabetes mellitus and chronic obstructive pulmonary disease presents with new-onset atrial fibrillation. Which of the following drug(s) would be the best choice for the management of rate control in this patient?
   a. verapamil
   b. sotalol
   c. esmolol
   d. all of the above

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4. Atrial fibrillation increases the risk of thromboembolic stroke by a factor of:
   a. 2 to 3
   b. 3 to 4
   c. 4 to 5
   d. 5 to 6

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5. A 70-year-old, otherwise healthy man with atrial fibrillation is being evaluated for anticoagulant therapy for prevention of thromboembolism. He is currently taking only metoprolol for rate control. The drug of choice for anticoagulation in this patient would be:
   a. warfarin
   b. aspirin
   c. heparin
   d. none of the above

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6. Genotyping patients for single nucleotide polymorphisms in VKORC1 and CYP2C9 may help in estimating the therapeutic dose of:
   a. digoxin
   b. warfarin
   c. amiodarone
   d. dronedarone

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7. Compared to warfarin, both doses of dabigatran in the RE-LY trial were associated with a higher risk of:
   a. myocardial infarction
   b. stroke
   c. systemic embolism
   d. all of the above

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8. Like direct thrombin inhibitors, oral factor Xa inhibitors offer the promise of anticoagulation that:
   a. is 100% effective
   b. does not increase the risk of bleeding
   c. does not require monitoring
   d. is inexpensive

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9. The treatment of choice for urgent conversion of atrial fibrillation to normal sinus rhythm is:
   a. anticoagulation
   b. catheter ablation
   c. DC cardioversion
   d. pulmonary vein isolation

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10. The most effective drug available for maintenance of sinus rhythm is:
    a. sotalol
    b. amiodarone
    c. dronedarone
    d. propafenone

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11. Adverse effects of dronedarone include:
    a. ocular toxicity
    b. hepatotoxicity
    c. thyroid toxicity
    d. none of the above

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12. Serious complications that can occur with pulmonary vein isolation include:
    a. atrial perforation
    b. cardiac tamponade
    c. thromboembolism
    d. all of the above

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