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Your Monthly Guide to Caring for Elderly Patients in the Emergency Department

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Atrial fibrillation (AF) is the most common, symptomatic sustained tachyarrhythmia that emergency physicians are faced with. Although most physicians consider AF to be a fairly routine and simple problem, its pathophysiology, potential complications, and management are complex and challenging. For older patients, management of AF requires assessing the underlying substrate; choosing the most appropriate pharmacologic agents; considering anticoagulation; and making appropriate disposition and referral decisions.[1]

Specific management strategies for AF include ventricular rate control coupled with anticoagulation vs. restoration and maintenance of normal sinus rhythm. Rate control is usually achieved pharmacologically with agents that block conduction through the atrioventricular node. Rhythm control may be achieved by electrical or pharmacologic conversion followed by pharmacolgic therapies to maintain sinus rhythm. Part I of this series covered strategies for rate control, emphasizing drug selection and dosages. This issue will offer an in-depth discussion of anticoagulation and restoration of sinus rhythm, with an emphasis on pharmacologic management. In addition, management of AF in special situations (myocardial infarction, Wolff-Parkinson-White [WPW] syndrome, thyrotoxicosis) and indications for hospitalization will be reviewed.

— The Editor

Atrial Fibrillation

Part II: Rationale for Anticoagulation and Recommendations for Restoring Sinus Rhythm

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Prevention of Thromboembolism

Anticoagulation is warranted if the patient is not certain of the time of onset of AF. Research suggests that thrombi can form within hours of AF onset. Furthermore, even after conversion to sinus rhythm, cardioversion may result in atrial stunning. Therefore, the patient may still develop interatrial clots, necessitating the use of coumadin for 4-12 weeks post-conversion; however, anticoagulation may be discontinued if the restored sinus rhythm persists for 2-4 weeks. In the past, thromboembolism after cardioversion has been attributed to dislodgement of preformed atrial thrombi during the resumption of atrial contraction. However, it appears that thromboembolism after cardioversion more often may be the consequence of the effects of cardioversion on atrial function.[2]

A stroke risk reduction of approximately 70% has been demonstrated in patients with nonrheumatic AF who are on oral anticoagulation.[3] Six major trials have demonstrated that the risk reduction associated with oral anticoagulation for stroke far outweigh the slight increase in annual risk of major hemorrhage: Atrial Fibrillation, Aspirin, Anticoagulation Study (AFASAK) from Copenhagen, Denmark; Boston Area Anticoagulation Trial for Atrial Fibrillation (BAATAF); Stroke Prevention in Atrial Fibrillation (SPAF) I, II, III;[4,5] Stroke Prevention in Non-rheumatic Atrial Fibrillation (SPINAF); Canadian Atrial Fibrillation Anticoagulation (CAFA); and European Atrial Fibrillation Trial (EAFT).[6]

Risk factors for stroke in AF include hypertension, diabetes, previous transient ischemic attack (TIA), systemic embolism or stroke, advancing age (1.4% for each decade), congestive heart failure (CHF), and global left ventricular dysfunction.[7-9]

Patients with structural heart disease, such as valvular heart disease or coronary artery disease, represent a high-risk group for thromboembolism.[10] Echocardiographic evidence of atrial or ventricular enlargement may pose a risk of embolization,[11] as well as represent a group of patients unlikely to remain in sinus rhythm after cardioversion. Pooled data from the first five of those studies listed previously (AFASAK, BAATF, SPAF I, SPINAF, CAFA) showed an annual risk reduction of 85% in AF patients older than 75 years with at least one risk factor, and a 51% risk reduction in AF patients older than 75 years with no risk factors. It is suggested that treating 1000 AF patients for one year will prevent approximately 30 strokes and seven deaths, at the cost of seven major bleeding episodes.

The risk of stroke rises when patients have international normalized ratios (INRs) of less than 2.0, whereas INR values of greater than 3.0 result in an increase in intracerebral hemorrhages.[3] No anticoagulation seems warranted in younger AF patients (< 60 years) without any clinical or echocardiographic risk factors. However, most patients with AF are older than 65 years of age and have such risk factors. Patients older than age 75 who had at least one risk factor had an annual stroke risk of 8.1%.[12] The decrease in prevalence of embolic events in anticoagulated AF patients has been known for decades.[13]

Advancing age is considered an independent risk factor for both intracerebral hemorrhage and subdural hemorrhage by some,[4,14] perhaps explaining why many elderly AF patients are under-anticoagulated despite strong evidence that warfarin therapy can prevent stroke. An analysis by the EAFT investigators indicated that warfarin was less effective in preventing stroke in patients older than 75 years.[15] It is apparent that the prevalence of AF continues to increase with age, as does the contribution of AF to stroke. Theoretically, very old (age > 80) patients may have even more to gain from warfarin therapy than patients younger than 80 years[16,17] because 36.2% of strokes in those ages 80-89 years have been shown to be AF related.[18] Yet one study found that only 32% of elderly AF patients who were residing in nursing homes and were eligible for warfarin therapy were receiving the medication.[19]

Clearly, for many physicians the risks of bleeding often prevail over the risk of stroke in elderly AF patients. Others have disputed the correlation between advancing age and hemorrhage, and posited that it is more critical to ensure that patients' INRs are reliably followed and maintained in the 2-3 range.[20] Anticoagulation services have been shown to improve rates of thromboembolism, reduce hemorrhagic complications, and relieve the individual practitioner of the logistic burdens of frequent monitoring and dosage changes.[21]

Transesophageal echocardiography (TEE) is more accurate than transthoracic echocardiography (TTE) for the detection of left atrial (LA) thrombus.[22] TEE has a reported sensitivity of 83-100% for the detection of LA thrombus when compared with operative findings as the reference standard.[23,24] It has been utilized in determining the need for and duration of anticoagulation before cardioversion in patients with AF.[25] It may demonstrate LA appendage thrombus and appendage dysfunction. As an indication of atrial stasis, swirling patterns in the LA appendage and LA fractional shortening may be observed. Spontaneous echodensities indicative of stasis, or "smoke," are described.[26] M-mode can assess left ventricle (LV) size and wall thickness.

In one study of 206 patients with AF, TEE was used for thrombus screening prior to cardioversion. In this group of patients screened with TEE, none of the patients developed a systemic embolus.[25] This same study also demonstrated that greater than five weeks of anticoagulation was required before LA thrombi either resolved or became immobile. Two other reports also noted no thromboembolic complications after pharmacologic or electric cardioversion of AF after short-term or no anticoagulation prophylaxis in patients with no atrial thrombus by TEE.[27,28] However, others have reported stroke or TIA in 5.6-6.7% of AF patients after cardiover-

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Table 1. Anticoagulation Guidelines in Atrial Fibrillation

IF AF > 48 HOURS DURATION, CONSIDER WARFARIN IF:

- Poor LV function
- Rheumatic heart disease or prosthetic heart valve
- Prior thromboembolism, TIA, or stroke
- Hypertension or DM
- Any patient > 65 years with no contraindications (i.e., risk of falls)
- If none of the above risk factors are present and patient is < 65 years, treat with aspirin, 325 mg/day.

IF AF < 48 HOURS DURATION AND CARDIOVERSION:

- Consider heparinization.
- Consider TEE to rule out thrombus or "smoke" prior to cardioversion.
  - — If contraindications to warfarin, use aspirin 325 mg/day.
  - — Anticoagulate with warfarin for 3-4 weeks post-cardioversion (electrical or chemical). If AF of unknown duration, anticoagulate for 3-4 weeks prior to cardioversion.

sion, despite having no thrombus detectable by TEE.[2,29] It is clear that thromboembolic complications may occur after cardioversion despite negative findings on preconversion TEE. Whether this is due to atrial stunning and subsequent hemodynamic stasis with thrombus formation following the procedure has not been ascertained. Since normal atrial contraction after cardioversion may take up to three months, prophylactic anticoagulation has been advocated for a variable period after cardioversion for AF.[2]

For patients who cannot tolerate warfarin, aspirin has been proposed as an alternative therapy for stroke prevention. Pooled data from three randomized trials utilizing 75-325 mg/day of aspirin indicate that the relative risk reduction for stroke in AF patients treated only with aspirin is approximately 21%, but with a 95% confidence interval of 0-38%.[12] A small effect of aspirin in AF patients is indicated.

In 1998, the American College of Chest Physicians and the American Geriatrics Society developed a set of practice guidelines for the medical management of patients with AF.[30,31] These guidelines, in agreement with the National Stroke Association's Stroke Prevention Advisory Board from 1999, recommend that:[7]

1. Long-term anticoagulant therapy (target INR of 2.0-3.0) strongly should be considered for all patients with AF who are older than 65 years.
2. Long-term anticoagulant therapy strongly should be considered for patients who are younger than age 65 and have any of the following risk factors: previous TIA or stroke, hypertension, diabetes mellitus (DM), history of systemic embolus, rheumatic mitral valve disease/mitral stenosis, prosthetic heart valve, or poor left ventricular function.
3. Patients who decline oral anticoagulant therapy or who are poor candidates for anticoagulation therapy should be given aspirin, 325 mg/day.
4. Patients younger than 65 years who have no risk factors for stroke can be treated appropriately with aspirin or no antithrombotic therapy. Lone AF has been shown to pose no greater risk for stroke by actuarial data than a matched, younger group without AF.[32]
5. For AF patients between the ages 65 and 75 years without additional risk factors, absolute risk reduction with either form of antithrombotic therapy (oral anticoagulation or aspirin), side effect profile, and inconvenience must be taken into account before selecting long-term treatment.

As with any other pharmacologic intervention in the elderly, older patients are more likely to be frail and prone to falling. They also may have comorbidities and levels of functional impairment (higher falls risk) that constitute contraindications to the use of warfarin. In addition, the elderly are more likely to use multiple medications, which can increase the likelihood of adverse drug interactions with warfarin. For patients older than age 75, the preferred target INR may be the lower end of the therapeutic range of 2.0-3.0.

Anticoagulation Recommendations

AF of Less Than 48 Hours Duration. If the patient requires emergency cardioversion, consider heparinization prior to cardioversion[28] and then coumadization for four weeks. When the patient requires elective cardioversion, consider giving heparin (the likelihood of emboli in AF of < 48 hours duration is low). Physicians may consider using TEE to search for inter-atrial thrombus, followed by anticoagulation with coumadin for 4-6 weeks post-cardioversion. *(See Table 1.)* Clinicians also may consider giving oral antiarrhythmics.

AF of Greater Than 48 Hours Duration. Three to four weeks of anticoagulation with coumadin is required before attempting cardioversion (target INR of 2.0-3.074). Use TEE to search for interatrial thrombus or "smoke";[33] if present, continue anticoagulation for 3-4 weeks before cardioversion. Also anticoagulate with coumadin for four weeks post-cardioversion.[26]

It should be noted that these recommendations for anticoagulation are for stroke prophylaxis. Other embolic complications which may ensue after AF include mesenteric ischemia or limb ischemia (which may require surgical intervention).

Recommendations for Restoration of Sinus Rhythm

There are many reasons for restoring sinus rhythm. These include:

- regularization of heart rhythm and rate;
- restoration of atrial contribution to cardiac output;
- improvement in hemodynamics;[34]
- maintenance of normal electrophysiology;
- prevention of LA dilation;
- prevention of left ventricular dysfunction and tachycardic-mediated cardiomyopathy;
- relief of symptoms and, possibly, improvement in life expectancy; and/or
- reduction in thromboembolic complications.[35]

Table 2. Vaughn Williams Classification of Drugs Used in Atrial Fibrillation

IA	Quinidine, procainamide, disopyramide
IC	Flecainide, propafenone
II	Propranolol, metoprolol, esmolol, atenolol
III	Sotalol, amiodarone, ibutilide, dofetilide
IV	Diltiazem, verapamil

MECHANISMS OF ACTION

IA	Decreases conduction velocity (QRS widening), causes prolongation of the action potential (QT prolongation).
IC	Markedly decreases conduction velocity.
II	Beta-adrenergic blockade, lowers sinus rate.
III	Prolongs action potential duration.
IV	Blocks calcium (slow) channel

Methods for Restoring Sinus Rhythm. In general, the likelihood of maintaining the patient in sinus rhythm should be considered prior to any type of attempted cardioversion. Chronic AF (> 12 months), severe LV dysfunction, mitral valve disease, rheumatic heart disease, sinus node dysfunction, and advanced age have been listed as markers of reduced likelihood of achieving or maintaining sinus rhythm.

The major risk of cardioversion is thromboembolism, with a 5% risk of stroke in the absence of anticoagulation.[13] Multiple drug failures, continued presence of acute precipitating factors, and left atrial enlargement greater than 5 cm are markers that diminish the likelihood of successful conversion. These markers are relative and are not absolute contraindications to cardioversion.[36]

Electrical Cardioversion. Synchronized electrical cardioversion should be performed in unstable AF patients (hypotension with end organ dysfunction or acute pulmonary edema) as is clinically warranted. The possibility that AF has been present chronically must be entertained, since cardioversion entails a risk of systemic embolization. Treating physicians also should recall that, in general, a rapid ventricular rate does not lead to hypotension, although this tachyarrhythmia may lead to impaired ventricular filling from decreased diastolic filling time, as occurs in mitral stenosis. Nonetheless, the hypotensive AF patient should be evaluated for intravascular volume depletion, including dehydration or blood loss. Drug-induced arterial dilatation, cardiac tamponade, cardiogenic shock, pulmonary embolism, and septic shock are other considerations.

In persistent AF, direct current (DC) cardioversion is effective for achieving sinus rhythm in 70-90% of patients.[37] It usually requires 50-350 J. In a study of 64 elderly patients, the rates of electrical cardioversion and long-term maintenance of sinus rhythm were similar to those of younger individuals.[38] In two other reports, electrical cardioversion was successful in 67-69% of elderly and 71-76% of younger patients, respectively, and multivariate analysis revealed that only duration of AF was associated with failure to establish sinus rhythm.[11,39] The rate of successful maintenance of sinus rhythm was significantly lower in elderly patients, however. Therefore, it has been suggested that electrical cardioversion should be avoided in AF patients older than age 70 who have an AF duration that exceeds 36 months and who have adequate exercise tolerance. Some drugs, such as ibutilide and digoxin, may reduce defibrillation thresholds, and their use has been proposed to facilitate defibrillation.[33]

Systemic embolization is a well-documented complication of electric or pharmacologic cardioversion in patients with AF, and is reported in 0.6-5.6% of patients undergoing cardioversion.[29] For this reason, a period of 3-4 weeks of anticoagulation prophylaxis has been recommended before cardioversion of AF of more than 48 hours duration.[40,41]

Electrical cardioversion of paroxysmal AF has been performed successfully in the emergency department (ED), with an 89% success rate.[41] Patients successfully converted to sinus rhythm safely may be discharged home. A nonfasting patient and those who may experience difficulty with sedation can be factors in the ED.

Internal cardioversion utilizes high energy (200-400 J) delivered between a right atrial (RA) cavity and a surface patch, or lower energy (2-20 J) delivered between RA and coronary sinus electrodes. It may be more effective than external cardioversion for restoring sinus rhythm in patients with persistent AF.[42] Implantable atrial defibrillators theoretically should be desirable in the hope that early conversion may prevent chronicity and morbidity due to AF, but defibrillation thresholds must be low enough to minimize discomfort. As well, they must have an accurate detection algorithm and have safety demonstrated by prospective studies.[33]

Pharmacologic Cardioversion

Pharmacologic cardioversion employs Class IA, IC, and Class III antiarrhythmics. *(See Table 2.)* These drugs prolong the refractory period of the reentrant wave fronts and impair conduction through the atrial tissue. The result is a reduced number of existing and new wave fronts. These agents also suppress automaticity, which has been implicated in some patients in the development of AF. By prolonging the refractory period or impairing conduction in the atria, they can reduce the number of propagating wavefronts, terminating and preventing the recurrence of AF. Each class will be considered in turn. Their overall success rate may approach 70% in restoring sinus rhythm. Ibutilide and procainamide have been cited as the most frequently used intravenous agents.[33]

Class IA Antiarrhythmics. Class IA agents slow conduction through the atria, AV node and His-Purkinje system directly, and decrease conduction in accessory pathways. Both quinidine and procainamide have peripheral vasodilatatory actions. Quinidine rarely is used because IV administration causes hypotension, and oral loading takes longer to convert AF. The oral dose is 200-400 mg 3-4 times per day (e.g., quinidine gluconate 330 mg every three hours up to a total of 990 mg). Side effects associated with quinidine are frequent and include gastrointestinal complaints, proarrhythmia (torsades de pointes), atrioventricular (AV) block, atrial flutter with 1:1 conduction, and sinus node suppression. Use

of quinidine has been associated with increased mortality in certain populations.[43,44]

Historically, procainamide has been the most common drug chosen for AF conversion. Conversion to normal sinus rhythm (NSR) occurs in approximately one-half of patients with AF, and restoration of NSR occurs even more frequently if AF has lasted for less than one day.[45,46] The loading dose of procainamide is 10-15 mg/kg IV given as 100 mg q 5 minutes, or up to 500-1000 mg over 10 minutes. The infusion should be stopped if the QRS or QT_c intervals exceed 130% of baseline or if systolic BP decreases by greater than 20%. This may be followed by a maintenance regimen of 2-5 mg/min IV infusion or 500-1000 mg q 8 hours orally.

Precautions. Proarrhythmic effects include torsades de pointes. Since a vagolytic effect may increase ventricular rate, many physicians give AV blockers first. Procainamide can induce hypotension and atrial flutter with 1:1 conduction.

Class IC Antiarrhythmics. Class IC agents markedly slow depolarization and conduction and are associated with significant antidysrhythmic properties.

Flecainide is only available in oral form in the United States. It has been used intravenously overseas, and has been effective in preventing recurrences of paroxysmal AF (68% event free after 4-8 weeks).[46,47] It may be optimal in facilitating conversion of AF patients with no structural heart disease.[33,48,49]

After rate control is achieved, 300 mg as a single oral loading dose is suggested. This regimen of flecainide 75-90% effective in converting AF to sinus rhythm within eight hours.[49,50] Maintenance dose is 50-100 mg bid or tid PO. Flecainide has been given intravenously as well, 1.5-2 mg/kg up to 150 mg, with a 57% conversion rate after one hour.[51]

Side effects of paresthesias, visual disturbances, vertigo, fatigue, dyspnea, hypotension can occur but are unusual. Adverse cardiac events, such as conduction disturbances, worsening of CHF, or development of malignant arrhythmias (e.g., ventricular tachycardia) are more common in patients with pre-existing structural heart disease. Exclusion criteria for use have included complete bundle-branch block (BBB), sick sinus syndrome, symptoms of CHF, or New York Heart Association functional class greater than 2, among others.

Propafenone is only available in the oral form in the United States. It is most effective when used for paroxysmal AF. Overall success rate for conversion to sinus rhythm from AF of recent onset is 57-91% within eight hours.[52-54] The suggested oral loading dose for propafenone is a 150-600 mg single dose,[11] with a maintenance dose of 450-900 mg given in three divided doses. Approximately 40-50% of AF patients who receive propafenone remain free of paroxysmal AF. Adverse effects include GI distress, a regular tachycardia with prolonged QRS and 1:1 AV conduction, ventricular tachycardia, and sinus node dysfunction. Propafenone has been used effectively to convert AF to sinus rhythm when given intravenously 2 mg/kg over 10 minutes and followed by slow infusion at 0.007 mg/kg/min. In one study of 98 patients with AF of less than seven days duration, NSR was restored in 91%.[54]

Precautions. Data from the Cardiac Arrhythmia Suppression Trial indicate that Class IC antiarrhythmic agents should not be administered to patients with severe underlying cardiac disease or when the QRS duration exceeds 120 msec.[55]

Class III Antiarrhythmics. Class III agents prolong the refractory period and action potential duration and have antifibrillatory properties.

Sotalol is not available in this country intravenously. It is less effective for converting AF than Class I agents, but more effective in maintaining sinus rhythm after conversion. Patients may have fewer symptoms with recurrent AF because of its beta-blocking activity. Sotalol has been used with digoxin for this reason to lower peak exercise heart rate, as well as for paroxysmal AF. The IV loading dose is 1.0-1.5 mg/kg over 10 minutes; it reduces ventricular rate in 10 minutes. The maintenance oral dose is 80-320 mg PO daily.[11] Sotalol has been associated with QT prolongation, polymorphic ventricular tachycardia (1.4%), and torsades de pointes. It should be used with caution in patients with CHF, renal insufficiency, and with pre-existing prolonged QT interval.

Amiodarone is available orally and intravenously. It prolongs refractoriness of atrial muscle and of the AV node. It also has beta-blocking and calcium channel blocking actions. Intravenous amiodarone is more effective for converting AF to NSR and controlling heart rate than digoxin, but central venous access is required for administration. IV administration may cause hypotension, AV block, and ventricular arrhythmias. Amiodarone is extremely effective for rate control even in patients with high catecholamine levels, as occurs with CHF.[47] Conversion success rates of 25-81% have been reported,[49,56] with an overall success rate of 71% when used for AF of less than 48 hours duration.[57]

In the acute setting, IV dosing of amiodarone is preferable to oral administration because of an extended loading period and a large side effect profile with PO dosing. IV dosage is 5-7 mg/kg diluted in 100 cc of normal saline (NS) infused over 10-40 minutes. A second loading dose may be given if there is no response to the first dose. Maintenance IV dose is 600-1200 mg over 24 hours titrated to ventricular response. It may be used in conjunction with digoxin for rate control. It may be used as first-line therapy in elderly patients with heart failure[11] and in paroxysmal AF to reduce the frequency of episodes and reduce the ventricular rate during episodes of AF. It was not as effective for conversion of AF (34%) as IV flecainide in one report.[47]

Precautions. Side effects include hypotension and flushing within minutes of administration, bradyarrhythmias, AV block, pulmonary fibrosis, liver, and thyroid toxicity. It may cause thrombophlebitis in smaller veins and is more effective if LA size is less than 4.5 cm.

Ibutilide is specifically approved for conversion of recent onset AF to NSR. It is available in IV form only, and it has a rapid onset and a short half-life of 60 minutes. Its mechanism of action is via delayed inactivation of the slow sodium channel, as well as by potassium channel blockade. Ibutilide converts 35-47% of recent onset AF.[33,58] No effectiveness has been determined with arrhythmias of more than 90 days dura-

Table 3. Patients at Risk for Antiarrhythmic Drug Proarrhythmia (Torsade de Pointes Markers)

- $QT_c \geq 460$ msec
- Active ischemia
- Advanced structural heart disease
- Hypokalemia
- Hypomagnesemia
- Severe bradycardia
- Ventricular stretch/hypertrophy

tion. Seventy percent of conversions occur within 60 minutes and one-half of these occur during infusion.[58]

The suggested loading dose of ibutilide is 0.01 mg/kg IV, up to 1.0 mg over 10 minutes; a second IV dose may be given after 10 minutes. No maintenance dose is given.

Precautions. Ibutilide may cause AV block and QT prolongation, and should not be given concomitantly with other drugs that prolong the QT interval. In 586 patients treated with ibutilide, sustained torsade de pointes occurred in approximately 2%, and nonsustained ventricular tachycardia was seen in another 7.6%.[59] Torsade de pointes usually occurs before conversion to NSR, and is more common if there is pre-existing left ventricular dysfunction. Patients should have serum magnesium checked prior to use, and should not have underlying bradycardia, hypotension, or CHF.

Dofetilide is a new compound developed mainly for maintenance of sinus rhythm after its restoration. Analysis of the Diamond Investigators of Arrhythmia and Mortality on Dofetilide (DIAMOND) trial showed dofetilide was effective for maintaining sinus rhythm in patients with depressed left ventricular function without increased mortality when compared with placebo.[60] Of patients in the DIAMOND study, 3.3% developed torsade de pointes, most often within the first three days of therapy. *(See Table 3.)* In the Symptomatic Atrial Fibrillation Investigation and Randomized Evaluation of Dofetilide (SAFIRE-D) study, 500 mcg twice daily for three days was used to achieve a conversion rate of 32% compared to 1% with placebo.[61] Dofetilide is contraindicated if the patient's QT_c interval is greater than 440 msec or the creatinine clearance is less than 20 mL/min. Currently used exclusively by cardiologists, it was effective in converting 15% of AF patients to sinus rhythm in one report.[62] Patients started on this agent must be admitted to a monitored setting for at least three days. The ideal patient for IV cardioversion with this agent is one with new-onset AF, a low likelihood of immediate recurrence, no torsade de pointes risk markers, and no need for maintenance therapy.[33]

Precautions. Any agents associated with potassium channel blockade can produce torsades de pointes and, therefore, should be administered only after hypokalemia, hypomagnesemia, and bradycardia have been addressed. In general, all Class I and III drugs have been shown to be more effective than placebo in maintaining sinus rhythm, and are effective in maintaining sinus rhythm for 6-12 months in approximately 50% of cases.[63]

The following guidelines have been proposed for determining optimal antiarrhythmic therapy in the management of AF, depending on the mechanism of the dysrhythmia and any underlying disease:[64]

If history suggests:
- Parasympathetic trigger: administer disopyramide;
- Sympathetic trigger: administer beta-blocker or sotalol; or
- No autonomic trigger: administer propafenone or flecainide

If patient is hypertensive: administer propafenone or flecainide.

If ischemic heart disease is present:
- And patient has normal LV function: administer sotalol;
- And patient has reduced LV function, but ejection fraction; (EF) is greater than 25%: administer sotalol, amiodarone, dofetilide, or beta-blocker; or
- And patient has severe LV dysfunction: administer amiodarone.

Special Situations

"Lone" Atrial Fibrillation. "Lone" AF occurs when the patient presents with AF that develops without underlying structural heart disease or other precipitating illness. Patients presenting to the hospital may be considered for electrical cardioversion or a Class III agent such as ibutilide, since anesthesia is avoided. If the patient is a reliable historian and the time of onset is certain, observation may be an option since approximately 50% of these patients will convert spontaneously;[65] if the patient does not convert spontaneously, they still will be within the 48-hour "window" for electrical or pharmacologic conversion. In general, patients should not be discharged on an antiarrhythmic drug after their first episode of AF unless high risk markers for recurrence are present or unless recurrence would pose a greater risk than antiarrhythmic therapy, as in syncope in a patient with hypertrophic cardiomyopathy.[63] For recurrent AF, the decision to be made is whether to control the rate or to convert. Patients with structurally normal hearts may be considered for single-dose therapy with a Class IC drug such as flecainide or propafenone orally for cardioversion after rate control.

Atrial Fibrillation in Myocardial Infarction. AF occurs in 6-23% of acute myocardial infarctions (AMIs),[66,67] AF often occurs within the first week following the infarction and most commonly affects elderly patients and/or those with large infarcts. This may be related to pericarditis, hypokalemia, hypoxia, increased catecholamine release, or to a hemodynamic burden on the atrium secondary to compromised left ventricular myocardium. There is small increase in short-term and long-term mortality when AF complicates AMI (relative risk of 1.18).[68] Patients with inferior AMIs may have a slow ventricular response and may not require any specific intervention.

American Heart Association recommendations for management of AF in AMI include the following:[26]

1. Electrical cardioversion in patients with severe hemodynamic compromise or intractable ischemia. However, there is a substantial risk of recurrence of AF, as well as atrial or ventricular stunning post-cardioversion.[69-71]

2. Rapid digitalization to slow a rapid ventricular response and improve LV function.
3. Intravenous beta-blockers to slow rapid ventricular response in patients without clinical left ventricular dysfunction, bronchospastic disease, or AV block.
4. Heparin should be given.

In terms of suppression of the arrhythmia after MI, sotolol and amiodarone have been proposed as safe agents.[63,72]

Atrial Fibrillation in Congestive Heart Failure. If the degree of heart failure is mild to moderate, rate control with diltiazem or digitalis may suffice. In severe CHF, AF may be problematic because the heart rate may be difficult to control safely. Diltiazem is a potentially negative inotrope[73] and digitalis is slow-acting. DC cardioversion carries the risk of ventricular stunning, hypotension, or bradyarrhythmias. The arrhythmia may recur after successful cardioversion.[69] Amiodarone has little negative inotropy, may control the ventricular response, and is relatively well tolerated.[74-76] Class IC agents should not be used.

Atrial Fibrillation in Wolff-Parkinson-White Syndrome (WPW). Ventricular pre-excitation occurs when a sinus impulse bypasses the AV node partially or completely and activates the ventricle through the anomalous pathway. Activation of the ventricles may occur via the AV node, by the accessory pathway, or by both pathways simultaneously. While supraventricular tachycardia with AV nodal reentry (AVNR) and narrow complex tachycardia is more common, AVNR may degenerate into AF. If the AV node is bypassed and the accessory pathway utilized, the accessory pathway may allow 1:1 conduction of atrial impulses to the ventricle. Therefore, the ventricular rate can accelerate to the atrial rate, approaching 300 beats/min with a rapid, wide, and irregular pattern. The rapid ventricular rate can degenerate to ventricular fibrillation (VF) and death.[77,78]

The treatment of choice in unstable patients or in those with a rapid ventricular response (> 250 beats/min) is electrical cardioversion.

If antiarrhythmic drugs are chosen because the patient is hemodynamically stable, procainamide in 100 mg boluses every five minutes up to 1 g slows conduction through the bypass tract and may chemically convert the rhythm to sinus.

Propafenone, a Class IC agent, and amiodarone, a Class III agent, are drugs used to slow the ventricular rate by selectively blocking the AV node. Digoxin and calcium channel blockers may accelerate conduction through the bypass tract, leading to dramatic increases in rate and hemodynamic compromise. Some advocate adding beta-blockers with AV nodal suppression.

After stabilization or conversion, the patient should be considered for possible radiofrequency ablation or surgical ablation of the anomalous tract.[79]

Atrial Fibrillation in Thyrotoxicosis. AF is the most common arrhythmia in thyrotoxicosis, occurring in 9-22% patients with this disorder. The incidence of AF increases with age. Patients may have pronounced palpitations due to increased blood volume, shortened circulation time, and decreased systemic vascular resistance. Thyroid hormone acts as a positive chronotrope, with increased cardiac output and stroke volume. The rapid ventricular rate and circulatory overload may precipitate CHF. There is an increased clearance of clotting factors, and a smaller dose of coumadin may be required to prevent embolization.

Beta-blockers represent the initial drugs of choice to control ventricular rate and symptoms. If CHF is present, esmolol may be more desirable than propranolol because of its short duration of effect if the drug must be discontinued. Stable patients with AF may be treated with oral beta-blockers. Standard treatment for CHF includes diuretics and preload and afterload reduction. Digitalis may be ineffective.

AF converts spontaneously to NSR in 62% of patients treated for thyrotoxicosis, though less frequently in patients with heart disease/dilated cardiomyopathy or long-standing AF. Elective cardioversion can be performed after the patient has been euthyroid for 8-10 weeks and anticoagulated. There is a high recurrence rate with DC cardioversion. Class 1A antiarrhythmics may be effective in maintaining NSR.

Postoperative Atrial Fibrillation

AF commonly follows coronary artery bypass graft surgery, although new-onset AF in this setting usually is transient. When AF reverts or is converted to sinus rhythm in this setting, it is unlikely to recur. No benefit and, perhaps, increased risk have been reported for antiarrhythmic agents. Standard treatment should consist of observation or control of ventricular response with an appropriate agent until AF relapses to sinus rhythm. Withdrawal of beta-blockers prior to surgery has been shown to increase the risk of developing AF,[80] and it is common to consider prophylactic perioperative use of beta-blockers. Beta-blockers also have been reported to be the drugs most effective in treating AF after coronary artery bypass surgery.[81] Heart rhythm should be monitored, especially if a Class I agent is administered.[82]

Non-Pharmacologic Modalities for Management of Atrial Fibrillation. Prophylactic atrial pacing is utilized in patients with paroxysmal AF or electrophysiologic evidence of interatrial conduction delay. Its chief benefit is found in patients whose AF is initiated by increased vagal tone, multiple atrial ectopic beats, or sick sinus syndrome. Patients without sinus disease but with severe sinus bradycardia and high vagal tone prior to onset of AF also are candidates.

Implantable atrial defibrillators utilize right atrial and coronary sinus leads. Dual chamber AV systems have been considered superior to single-chamber ventricular demand pacemakers.[83] Success rates for defibrillating AF have been cited at 96%.[84] In paroxysmal AF, typically 0.5-5.0 J are needed. For chronic AF, more than 5.0 J may be necessary.

The key concept for implantable defibrillators is that by preventing the atria from remaining in AF, remodeling in the atria is prevented. Single chamber and dual chamber defibrillators are being investigated.[26] Newer pacing methods, such as biatrial pacing, also are being studied, as well as appropriate detection of AF for delivering shocks. Patients may feel chest pain, and shocks may be frequent. Microscopic hemorrhage or

Table 4. Indications for Hospitalizing Patients with Atrial Fibrillation

- Suspicion of ischemic heart disease/acute coronary syndrome
- Management of congestive heart failure
- Any noncardiac disease that mandates admission:
  — Infective endocarditis
  — Systemic emboli
  — Gastrointestinal bleeding
  — Myocardial contusion
- Any patient started on a Class IA antidysrhythmic agent
- Hypotension, hemodynamic instability, heart rate > 140 beats/min
- Syncope
- High risk of thrombus formation: prosthetic mitral valve
- Suitability for chemical or electrical cardioversion

thrombosis at the site of the defibrillation has not yet been determined to be clinically significant.

Surgical Therapy

There have been two surgical techniques described for definitive treatment of AF, the maze and the corridor procedures.

Maze Procedure. This is a surgical procedure that has been used to restore sinus rhythm and prevent recurrent episodes of AF. Since there is a critical atrial tissue mass necessary to sustain AF, when multiple incisions are performed in both atria and bilateral appendectomies, a series of dead-ends for wavelets is created. Sinus impulses are made to channel through a path, or "maze," to reach the AV node. AF cannot be maintained, and the atria revert to normal sinus rhythm. First described in 1991, it has been modified several times.[85]

Since this requires open heart surgery, it is reserved for drug refractory AF or for failed AV node ablation therapy. The operation has a 3% surgical mortality, and patients may require a pacemaker. Its success has been reported to be in the 84-98% range, with 71-91% of patients not requiring pharmacologic treatment following this operation.[86]

Corridor Procedure. This procedure creates a sleeve of right atrial tissue or "corridor" connecting the sinus node to the AV node.[87] It allows impulse conduction from the sinoatrial (SA) node directly to the AV node and protects the AV node from a rapid fibrillatory rate.[88] Unfortunately, while it restores sinus node control of the ventricles, the loss of atrial transport and of AV synchrony entails a continued risk of thrombus. Because of this and more effective pharmacologic and surgical therapies, this procedure has fallen out of favor.[63]

Catheter Ablation. First described in 1994, radio frequency energy can be used to ablate or to modify the AV node.[89] Complete atrioventricular block usually can be produced via radio frequency current delivered to the right side of the heart; if not, a left ventricular approach almost always will be successful. Patients will require a permanent pacemaker after AV node ablation.

AV node modification is performed by delivering radio frequency energy in the right atrial posterior septum or mid-septum. The goal of atrioventricular node modification is to control the ventricular rate without creating high-grade AV block. Twenty-five percent of patients end up requiring a permanent pacemaker after AV node modification.[90,91] The atria continue to fibrillate, and loss of AV synchrony may pose a risk of intra-atrial thrombus. There is still a need, therefore, for anticoagulation.[26]

A catheter version of the maze procedure has been performed by creating several linear lesions in the left or right atrium. The goal is similar to the maze procedure, that is, to compartmentalize the atrium by creating transmural linear lesions in the atrial myocardium that will block the wave fronts. When enough atrial tissue is compartmentalized, AF cannot be maintained. A problem with the procedure is that RA ablation alone does not eliminate AF; interatrial tachycardias may develop after ablation of tissue. Radiofrequency causes heat in atria, potentially leading to atrial charring and thrombus formation.

Admissions Decisions: The Bottom Line

Medically justified admissions for AF have been evaluated retrospectively,[92] and it was determined that 98% of patients with AF whose admissions were medically justified could have been identified in the ED. These patients had electrolyte abnormalities, CHF, chest pain suggestive of myocardial ischemia, hypotension, or noncardiac diseases that necessitated admission. *(See Table 4.)* A case can be made, however, that all new-onset AF should be converted to normal sinus rhythm as soon as possible. Patients who are cardioverted in the ED to sinus rhythm need not be hospitalized any longer than it takes to recover from their procedural sedation. However, if Class IA antidysrhythmic agents are used, the patient should be observed for 72 hours for torsade de pointes associated with QT prolongation.[93]

Other indications for hospitalizing patients who are in AF include those with decompensated CHF, myocardial contusion, infective endocarditis, hypotension, syncope, or other medical reasons for hospitalization independent of the AF. Recently, recommendations for hospitalization for AF have been reviewed from an HMO perspective.[94] Hospitalization was deemed necessary if the patient was hemodynamically unstable or symptomatic from ischemia or from CHF. Patients who represent an unusual anticoagulation or embolic risk are also recommended for immediate hospitalization. Examples would include patients with recent history of gastrointestinal bleeding and patients with prosthetic mitral valves and new-onset AF, respectively.[95]

On the other hand, outpatient management is preferred if patients are deemed to have permanent AF with no consideration for conversion, whose therapy, therefore, will consist of rate control and anticoagulation. Patients with recurrent paroxysmal AF whose episodes have reverted spontaneously to sinus rhythm, or if AF is chronic (> 1 week), who are already on anticoagulation, usually can be managed as outpatients.

A "gray zone" may include patients who are asymptomatic, but whose AF is of unknown duration or of recent onset. Patients with heart rates of greater than 140 beats/min for example, would not, in general, be discharged from the hospital.[94]

Summary

AF management is not straightforward; it is a complex disorder. Treatment strategies vary by patient, and optimal therapy for each patient in AF has not been defined. Selection of any agent to control rate vs. rhythm conversion and maintenance will depend upon its side effect profile, the clinical urgency, and the patient's hemodynamic status. For patients with infrequent and non-life-threatening episodes, intermittent cardioversion will have less adverse impact on their daily lives and less adverse risk than would daily antiarrhythmic therapy. Antiarrhythmic drugs may prevent recurrent AF, but most are only modestly effective, and none are uniformly safe. Only selected patients require restoration and maintenance of normal sinus rhythm. Elderly patients who remain in AF are at significant risk for embolic stroke and require anticoagulation unless there are medical or social contraindications for warfarin therapy. The decision to admit will depend upon the presence of cardiovascular instability, the presence of comorbidities, and the patient's suitability for chemical or electrical cardioversion.

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Physician CME Questions

18. Which one of the following statements is *incorrect*?
    A. Atrial stunning persists after cardioversion.
    B. Thrombi can form within hours of atrial fibrillation onset.
    C. Thromboembolism after conversion to sinus rhythm more often may be the consequence of the effects of cardioversion on atrial function.
    D. Coumadin is *not* necessary after cardioversion to sinus rhythm, if the patient has been anticoagulated for four weeks prior to cardioversion.
    E. Anticoagulation should be continued for several weeks after AF of recent onset is converted to normal sinus rhythm.

19. In patients with nonrheumatic atrial fibrillation, the approximate stroke risk reduction from oral anticoagulation is:
    A. 10%.
    B. 25%.
    C. 40%.
    D. 50%.
    E. 70%.

20. Risk factors for stroke in patients with AF include which of the following?
    A. Previous transient ischemic attack (TIA)
    B. Advancing age
    C. Global left ventricular dysfunction
    D. Structural (valvular) heart disease
    E. All of the above

21. Which is of the following is *incorrect* regarding anticoagulation for atrial fibrillation?
    A. The risk of stroke increases with INR of less than 3.0.
    B. The risk of bleeding increases with INR of greater than 3.0.
    C. No anticoagulation seems warranted in AF patients younger than 60 years of age without risk factors.
    D. The risk of stroke increases with INR less than 2.0.
    E. The risk reduction of stroke becomes more marked with increasing age of the patient.

22. Regarding echocardiography for atrial fibrillation patients, which of the following is correct?
    A. With operative findings as the reference standard, the sensitivity of transesophageal echocardiography (TEE) for detection of thrombi is 60%.
    B. M-mode can assess LV (Left ventricular) size and wall thickness.
    C. Transthoracic echocardiography (TTE) is more sensitive for detection of thrombus than is TEE.
    D. If there is no thrombus on TEE, it is completely safe to cardiovert a patient in chronic AF.
    E. A normal TEE and TTE predicts normal atrial function for weeks after cardioversion.

23. The guidelines published by the American College of Chest Physicians and the American Geriatrics Society indicate that:
    A. Patients who decline oral anticoagulant therapy should be given long-term low molecular weight heparin subcutaneously.
    B. Patients who are in "lone" AF and are between the ages of 55 and 60 with no risk factors should always receive aspirin 325 mg/day.
    C. Patients who are poor candidates for anticoagulant therapy and are older than 65 years should be given aspirin 325 mg/day.
    D. Patients ages 65-75 years old with AF and no additional risk factors should be anticoagulated regardless of side effect profile or convenience.
    E. It is well-documented that any elevation of INR is desirable, even if subtherapeutic (INR < 1.5) in preventing stroke.

24. Which of the following is *not* appropriate in the cardioversion of a patient in AF for more than 48 hours?
    A. Three to four weeks anticoagulation with warfarin prior to cardioversion
    B. TEE to search for interatrial thrombus or "smoke"
    C. Anticoagulation with warfarin for four weeks post-cardioversion
    D. Anticoagulation with subcutaneous heparin for 3-4 weeks prior to the cardioversion
    E. Follow-up for other thromboembolic complications, such as mesenteric or limb ischemia

25. A patient arrives in atrial fibrillation who has a ventricular response of 240 beats/min. His blood pressure is 110 systolic, and he is alert. On his EKG you see a wide complex QRS and diagnose Wolff-Parkinson-White syndrome. You feel that he is hemodynamically stable to administer an antiarrhythmic agent. You should choose which of the following?
    A. Diltiazem to slow his ventricular response
    B. Digoxin to block conduction through the AV node
    C. Esmolol to slow the heart rate in a controlled fashion
    D. Procainamide to block conduction in the accessory pathway
    E. Dofetilide as the newest agent for AF on the formulary

In Future Issues:

Abdominal Aortic Aneurysm