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Emergency Medicine Reports™

Volume 19, Number 23

November 9, 1998

Emergency department physicians encounter atrial fibrillation (AF) in a variety of presentations, ranging from chronic, well-managed, asymptomatic disease to acute hemodynamic compromise associated with a rapid ventricular rate. The emergency department (ED) physician must investigate not only the underlying causes and precipitants of AF, but must also perform a risk assessment concerning the possibility of acute ischemia and determine the need for admission. Furthermore, issues concerning anticoagulation and prevention of thromboembolism must be addressed.

To make matters more complicated, a variety of new strategies and drugs have appeared for rapid rate control and immediate chemical cardioversion. For the patient with AF who is unstable due to decompensated heart failure, acute ischemia, or hypotension, a number of management options are available, and decisions concerning electrical cardioversion are not as straightforward as they are in supraventricular tachycardia (SVT), ventricular tachycardia, or ventricular fibrillation. This review presents targeted strategies for ED evaluation and management of AF. New therapies for acute rate control, chemical cardioversion, and other approaches for the unstable patient are highlighted.

—The Editor

Atrial Fibrillation: Targeting Therapy and Risk Stratification Strategies for Patient Management

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Background

AF is the most common sustained cardiac arrhythmia, with a prevalence of about 0.5-1.0% in the population at large.[1-3] With advancing age the prevalence increases, with 5% of patients older than age 65 having AF.[1-4] Chronic AF is a major risk factor for stroke, carrying a risk of about 3-7% per year in older patients with associated coronary heart disease or CHF who are not receiving coumadin.[5]

The presence of AF indicates a high likelihood of coexisting cardiovascular or systemic disease. Underlying conditions capable of producing AF include hypertensive heart disease, coronary artery disease, valvular heart disease, cardiomyopathies, pericarditis, congenital heart disease, cardiac contusion, Wolff-Parkinson-White syndrome (or other accessory pathways), and cardiac surgery.[5] Systemic conditions associated with atrial fibrillation include thyroid disease, malignancy, ethanol intoxication and withdrawal, severe electrolyte disturbance, sarcoidosis, amyloidosis, pheochromocytoma, and pulmonary embolism.[5,6] About 10% of patients with AF have no associated disease, and are referred to as having lone AF.[7]

The duration of new onset AF varies considerably, with about 30-60% of patients converting spontaneously to sinus rhythm within 24 hours.[8-10] The duration is important, in part, because persistence of the arrhythmia produces electrophysiologic changes in the atria, or "remodeling," that increases the likelihood that the arrhythmia will continue.[11] More importantly, the duration of the arrhythmia is related to the risk of thrombus formation. Patients with AF lasting longer than 48 hours are at risk for developing an atrial thrombus and should not undergo elective attempts at chemical or electrical cardiover-

sion unless they have received adequate anticoagulation.[12] In contrast, patients with brief intermittent episodes of AF in the absence of structural heart disease carry a much lower risk of cardioembolic stroke.[12]

Clinical Features

Patients with new onset AF typically present with symptoms of rapid heart rate, palpitations, and/or shortness of breath. In the absence of underlying conduction system disease, the ventricular response is rapid—usually in the range of 100-160 beats per minute. A pulse deficit is usually present; in other words, the radial pulse is slower than the auscultated apical rate because some of the ventricular contractions, due to inadequate filling times, are not strong enough to transmit a pressure wave to the radial artery.[13]

It should be stressed that patients with slow rates that are not attributable to medications inhibiting AV node conduction may have underlying conduction system disease that will increase the risk of severe bradycardia upon cardioversion. On the other hand, a very rapid (> 160) ventricular rate, accompanied by a wide QRS suggests the presence of an accessory pathway. Normalization of the rate in patients with preexisting AF suggests the possibility of atrial tachycardia, junctional or idioventricular rhythms, or ventricular tachycardia, all of which may result from digoxin toxicity.

Clinical evaluation of patients with AF should include a search for underlying structural heart disease (especially cardiac ischemia) and for systemic conditions that may precipitate the arrhythmia. The history should note the presence of alcohol or illicit drug use, risk factors for coronary artery disease, and symptoms of angina and congestive heart failure. A history of syncope is important because it may be a clue to the presence of sick sinus syndrome or nonsustained ventricular tachycardia. Detection of noncardiac illnesses also are important and may affect management decisions. Evidence of congestive heart failure, valvular heart disease, pericarditis, or thyrotoxicosis should be sought.

Diagnostic Studies

The electrocardiogram is valuable for a number of reasons. First, it will confirm the diagnosis by the presence of irregularly irregular supraventricular beats without discernible P waves. Fibrillatory waves (F waves) may be present and appear as fine, irregular undulations of the baseline, which are sometimes mistaken for flutter waves. Ashman's phenomenon is a transient bundle branch block that produces a wide QRS complex when a long R to R interval is followed by one that is short. Look for electrocardiographic evidence of acute ischemia, new or old infarction, pericarditis, and ventricular hypertrophy. Patients taking digoxin may have characteristic ST depression. Patients taking quinidine or other class IA antiarrhythmic drugs may have QT prolongation.

Additional studies that may be helpful in the ED include a chest x-ray, which may reveal cardiomegaly, congestive heart failure, pneumonia, chronic obstructive pulmonary disease (COPD), tumors of the lung and mediastinum, or evidence of pulmonary embolism as causative or complicating factors. Look for and correct serum electrolyte abnormalities. An elevated creatinine is important to note because digoxin is, in part, renally cleared. If the patient is taking warfarin, check the prothrombin time to make sure the INR is in the range from 2 to 3.

Transthoracic echocardiography, although extremely valuable in the work-up of patients with AF, is deferred to the outpatient setting, or may be performed later in the course of the patient's hospitalization, if admitted. Similarly, a screening thyroid study can be done as an outpatient since results would not be available in the ED.

Slowing the Ventricular Response in AF: Rate Control in the Emergency Department

Digoxin. A number of agents are available for rate control in the ED setting. *(See Tables 1 and 2.)* Digoxin, the most commonly prescribed cardiac glycoside, is the oldest drug in use for control of the ventricular response in AF. Digoxin inhibits the active transport of sodium and potassium across cell membranes. Inhibition of the sarcolemma ATPase results in an increase in cytoslic calcium, thus increasing the force of

Emergency Medicine Reports™ (ISSN 0746-2506) is published biweekly by American Health Consultants, 3525 Piedmont Road, N.E., Six Piedmont Center, Suite 400, Atlanta, GA 30305. Telephone: (800) 688-2421 or (404) 262-7436.

Publisher: Brenda Mooney
Managing Editor: David Davenport
Copy Editor: Suzanne Zunic
Marketing Manager: Deb Zelnio

GST Registration No.: R128870672

Periodical postage paid at Atlanta, GA. **POSTMASTER:** Send address changes to ***Emergency Medicine Reports***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $21. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Multiple copy prices: One to nine additional copies, $87 each; 10 or more additional copies, $58 each.

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1 year *with* 52 ACEP/AMA/52 AAFP Category 1/Prescribed credits (52 AOA Category 2B credits): $387
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Table 1. Targeted Strategies for Rate Control in Atrial Fibrillation

PATIENTS WITH MILD OR MODERATE HEART FAILURE AND NORMAL TO HIGH BLOOD PRESSURE	
Diltiazem IV	Expensive, bolus wears off quickly, needs to be followed with a continous infusion
Digoxin IV	Inexpensive, does not cause hypotension, onset of action > 4 hours
PATIENTS WITH SEVERE HEART FAILURE (WHO HAVE FAILED CARDIOVERSION)	
Digoxin	Slow in onset, > 4 hrs
Amiodarone	Slight risk of extreme bradycardia
PATIENTS WITH SEVERE CHF, VOLUME OVERLOAD, AND SIGNIFICANT HYPOTENSION (WHO HAVE FAILED CARDIOVERSION)	
Digoxin	With pressor support (phenylephrine or norepinephrine)
Amiodarone	With pressor support
PATIENTS WITH ISCHEMIC CHEST PAIN OR ACUTE MI (IN PRESENCE OF ONGOING ISCHEMIC PAIN, EMERGENCY DC CARDIOVERSION SHOULD BE PERFORMED)	
Metoprolol IV	Has advantage of decreasing mortality in acute MI
Diltiazem IV	Fairly easy to titrate, some protection against ischemia
WPW AND RAPID AF	
Procainamide	Slows rate through the bypass tract while converting to sinus. (Do not give digoxin, calcium blockers, or beta blockers! They may increase conduction through the bypass tract.)
THYROTOXICOSIS	
B blocker IV	If the patient has concurrent high output CHF, choose esmolol because of its short half-life; otherwise may give propranolol
PATIENTS WITH RAPID RATES AND HYPERTENSION	
Verapamil IV	Less expensive than diltiazem, but with more negative inotropy
Metoprolol IV	Also a potent negative inotrope

Table 2. Dosages of Drugs for Rate Control in Atrial Fibrillation

DIGOXIN

0.5 mg IV, then 0.250 mg in one hour (max 1-1.5 mg/24hr)

DIGOXIN AND MAGNESIUM

0.5 mg digoxin IV, 2 gm $MgSO_4$ bolus, then 1 gm $MgSO_4$/hr X 4 hours

DILTIAZEM

0.25 mg/kg IV bolus, 15 min later if needed give second bolus 0.35 mg/kg, then 5-15 mg/hr maintenance

PROPRANOLOL

1 mg IV, repeat in 5 minutes if needed

METOPROLOL

5 mg IV, repeat in 5 minutes if needed

ESMOLOL AND DIGOXIN

0.25-0.5 mg digoxin, repeated in 2 hours

Esmolol dose titration:

Time (min)	IV Bolus (mg)	IV Infusion (mg/min)
0	10	2
5	10	4
10	20	8
15	20	12
20	20	16

VERAPAMIL

2.5-5mg IV, repeat in 30 minutes if needed

myocardial contraction. In specialized conduction cells, including those of the AV node, digoxin causes a *decrease* in automaticity and increases the maximal resting diastolic membrane potential, primarily due to digoxin's vagotonic effects. The effective refractory period in the AV node is increased, and conduction velocity is decreased.[14,15] The clinical result is a decrease in ventricular rate.

Patients with congestive heart failure have chronically elevated sympathetic tone and decreased baroreceptor responsiveness. The infusion of digoxin in the setting of heart failure decreases sympathetic tone by increasing carotid baroceptor responsiveness and by increasing cardiac inotropy. The result is a lower blood presssure with a higher cardiac output. Although the use of digoxin does not prolong life in patients with congestive heart failure, its use has been clearly shown to lessen symptoms and to decrease the likelihood of hospitalization.[16] As a result, digoxin is one drug of choice for rate control in AF patients with moderate to severe heart failure.

However, there are two principal drawbacks to the use of digoxin in the ED. The first has to do with its slow onset of action.[17] Of the various protocols for intravenous loading of digoxin, none demonstrates significant slowing of the ventricular response until about four hours or more have passed. Second, digoxin does not prevent adrenergic increases in heart rate.[18] As a result, many ED patients who have a high degree of sympathetic tone (due to pain, respiratory distress, anxiety, alcohol withdrawal, etc.) will not achieve adequate rate control with digoxin. And those ED patients who are sent home on digoxin may be aware of a rapid heart rate upon mild to moderate physical exertion.

Other potential problems with digoxin result from its narrow therapeutic range, toxic effects, and potential drug interactions. Digoxin also has a long elimination half-life (approximately 36-48 hours), and high levels will accumulate in patients with impaired renal function unless dosage and dosing interval are adjusted accordingly. In general, clinical benefit from digoxin in heart failure is seen with serum levels about 1 ng/mL, with an optimal effect at 1.3 ng/mL, although the dose reponse is nonlinear. Unfortunately, in AF, the relationship between dose and response is not as predictable. Clinical signs of toxicity are typically seen with levels of 2-3 ng/mL or higher, although there are some patients who may have evidence of mild toxicity at lower levels. Symptoms of toxicity include confusion, malaise, visual disturbance (intense yellow colors, halos), nau-

Table 3. Transition from Intravenous to Oral Diltiazem

INFUSION RATE	ORAL DILTIAZEM CD DOSE
5 mg/hr	180 mg
10 mg/hr	300 mg
15 mg/hr	360 mg

The infusion is continued for 4 hours after the oral dose is given. Alternatively, one may use short-acting diltiazem at doses of 30, 60, and 90 mg, respectively, with discontinuation of the infusion 2-4 hours later.

sea, vomiting, abdominal pain (which in some cases is due to mesenteric ischemia caused by digoxin-mediated reduction in splanchnic blood flow), cardiac arrhythmias, especially exccessive slowing of the ventricular response, and accelerated junctional rhythms. Important drug interactions include decreased digoxin clearance with concurrent administration of quinidine, amiodarone, captopril, diltiazem, nifedipine, or verapamil.[14,15]

Hypomagnesemia is known to attenuate the cardiac response to digoxin. Clinical trials have examined the effects of ventricular rate control when intravenous digoxin is given concurrently with intravenous magnesium.[14-16] The results of these clinical trials indicate that the combination of magnesium and digoxin is superior to digoxin alone in achieving rate control.[19,20] Whereas intravenous loading protocols for digoxin may take more than four hours to slow the ventricular response, the *combination* of digoxin and magnesium can achieve a 25% reduction in heart rate in 2-4 hours. Accordingly, if one chooses intravenous digoxin for rate control, magnesium should be added in all patients with known or suspected magnesium deficiency, such as alcoholics, or individuals receiving potent doses of loop diuretics. Do not give magnesium in the the setting of renal insuficiency or renal failure, since toxic doses of magnesium will accumulate rapidly. Even in patients with normal renal function, extremely high doses of magnesium (e.g., 10 gm given intravenously over 6 hours) can cause dangerous pauses.[20]

Beta-Blockers. Beta-1 adrenergic receptor *stimulation* of the heart causes increases in rate, myocardial contractility, conduction velocity, and automaticity. *Blockade* of the beta-1 receptor produces slowing of AV conduction and increased AV node refractoriness which, in AF, results in slowing of the ventricular response. Concommitant decreases in cardiac contractility can result in hypotension or congestive heart failure. Beta-2 receptor blockade may lead to bronchial smooth muscle constriction, and, in diabetic patients, may delay recovery from hypoglycemia because of catecholamine effects on glycogenolysis.[21]

Intravenous beta blockers can produce rapid control of the ventricular response in AF. The beta blockers, metoprolol, propranolol, and esmolol, are available for intravenous administration.[18] Esmolol, which is metabolized by red cell esterases, has the shortest elimination half-life (9 minutes) and selectively blocks B1 receptors. Esmolol is metabolized to methanol; however, the amount of methanol produced is not significant, and methanol toxicity does not occur. Esmolol's extremely short half-life makes it desirable when there is a risk of hypotension or heart failure. Propranolol blocks both beta-1 and beta-2 receptors and has a plasma half-life of about 3-5 hours. Metoprolol has beta-1 selectivity and has a plasma half-life of about 3-4 hours. Intravenous beta blockers usually are contraindicated in the settings of congestive heart failure, reactive airway disease, and hypotension.

Early studies of esmolol for rate control in AF and atrial flutter reported a 12-48% incidence of hypotension.[18] A subsequent study used esmolol in combination with digoxin in an attempt to minimize the hypotensive and negative inotropic effects of esmolol.[22] Of 21 patients studied, no episode of symptomatic hypotension occurred, and there were only two cases of dyspnea or congestive heart failure. Because no comparison treatment arm was used, it is not known whether the combination of esmolol and digoxin is superior to esmolol alone, either in terms of efficacy or in terms of complication rates. If esmolol is used in AF, a less aggressive dosing protocol should be used than that recommended, in order to minimize the risk of hypotension. When contraindications are absent, intravenous beta blockers are the drugs of choice for rate control in patients with thyrotoxicosis, alcohol withdrawal, hypertension, and in those with a history of angina pectoris or prior myocardial infarction.

Calcium Channel Blockers. The introduction of calcium channel blockers has dramatically improved management of AF. Excitation-contraction coupling in the heart depends on the activation of fast sodium and slow calcium channels. Calcium entering myocytes binds to troponin, freeing actin and myosin to contract. As a result, all calcium channel blockers have the potential to cause negative inotropy. In vascular tissue, increases in cytosolic calcium lead to contraction of smooth muscle. All classes of calcium channel blockers cause a decrease in arterial smooth muscle tone. They do not have significant effects on venous beds and do not increase venous capacitance or diminish preload.

AV node conduction depends, in part, on the rate of recovery of the calcium slow channel. The dihydropyridine calcium channel blockers (e.g., nifedipine) do not block the rate of recovery of the slow channel and consequently do not slow AV conduction. Verapamil (a phenylalkylamine calcium channel blocker) and diltiazem (a benzothiazepine) both decrease the rate of recovery of the slow channel, slowing conduction through the AV node. Verapamil and diltiazem may be associated with negative inotropic effects.[15,23]

When given intravenously, verapamil produces lowering of arterial blood pressure due to direct vasodilatation. There is also a blunting of the reflex tachycardia due to verapamil's negative chronotropic effects. The negative inotropic effects of verapamil are partly compensated by reduction in afterload. In patients with congestive heart failure, verapamil may cause profound hypotension due to diminished cardiac contractility and peripheral vasodilitation. However, in patients *without* preexisting left ventricular dysfunction, verapamil is generally safe and effective in controlling rate; symptomatic hypotension is rare even in otherwise healthy individuals.[24] Diltiazem has a similar effect on the AV node, but it is associated with less negative inotropy, making it a safer drug in patients with borderline low blood pressure or mild-to-moderate congestive heart failure.[25] As a general rule, verapamil is appropriate for rate control in the

patient with hypertension and rapid AF, but who has no history of congestive heart failure. Diltiazem is ideal in the normotensive patient, and in the patient with mild-to-moderate heart failure who requires rapid rate control.

The use of diltiazem in the setting of heart failure is not entirely without risk, because there is a small incidence of hypotension.[25] Consequently, diltiazem should not be used in patients with preexisting hypotension or severe heart failure because of the risk of producing shock. One should also bear in mind the financial considerations related to the use of intravenous diltiazem. It is more costly than verapamil. And because of its short duration of action, an initial bolus must be followed by a continuous infusion, requiring nursing monitoring in the ED or, subsequently, in the CCU.

The transition from intravenous to oral diltiazem may take hours to achieve.[26] One protocol for the transition from intravenous to oral diltiazem has been described in the literature. *(See Table 3.)* Patients who were stable for two hours on an intravenous infusion of diltiazem were given a dose of long-acting oral diltiazem (diltiazem CD) based on the IV infusion rate. The infusion was stopped four hours after administration of the oral dose. Seventy-seven percent of patients maintained heart rate control during the transition period.

Unstable Patients with Rapid AF

The Patient With Acute Myocardial Infarction (AMI). The patient with AF in the setting of an acute myocardial infarction (AMI) frequently presents a management problem. The incidence of new onset AF in CCU patients with acute infarction is roughly 11-19%.[27,28] In anterior infarction, the arrhythmia may result from diminished left ventricular contractility with subsequent rise in left atrial pressure. In inferior infarction, AF is frequently associated with right ventricular infarction. In selected cases of transmural infarction, AF results from acute pericarditis.[29] Some patients with acute infarction have chronic or paroxysmal AF or comorbidities that predispose to AF such as hypertension or pulmonary disease.

ACLS guidelines recommend immediate electrical cardioversion for patients with serious signs or symptoms; however, these recommendations bear some consideration in the patient with AMI. In some patients with AMI, AF is *chronic*, and there will be a substantial risk of thromboembolism with DC cardioversion if adequate anticoagulation has not been maintained. These patients require immediate rate control with a beta blocker or calcium channel blocker. In patients with *new onset* AF, the arrhythmia frequently converts spontaneously within a short period of time.[27,30] The ventricular response is not always rapid, especially in the setting of inferior infarction, and may not require specific intervention.[31]

For those patients with acute infarction and rapid ventricular rates, success has been reported with the use of intravenous propranolol.[32] Propranolol and metoprolol both have long half-lives, posing a slight risk of prolonged bradycardia. However, early intravenous beta blocker therapy has been shown to decrease mortality in AMI. Esmolol, because of its short half-life, would, in theory, be slightly safer than propranolol or metoprolol. Because of the paucity of published data, however, the routine use of intravenous beta blockade over direct current cardioversion in the acutely infarcting patient cannot be recommended. Intravenous beta blockers would be appropriate in the patient who has failed cardioversion, or in the patient who has a rapid rate without ongoing ischemic chest pain.

Intravenous amiodarone has also been studied in patients with acute atrial fibrillation complicating myocardial infarction, and has the advantage of both achieving rapid slowing of the ventricular response, as well as restoring sinus rhythm in the majority of patients.[33,34] Although complications are rare, amiodarone can cause worsening of congestive heart failure and excessive slowing of the ventricular response.

DC cardioversion is clearly justified in patients with persistent ischemic chest pain and a rapid ventricular response. The risks of DC cardioversion are low; however, cardioversion can result in atrial or ventricular stunning (causing or exacerbating heart failure), inappropriate bradycardia, ventricular tachycardia, and, in rare cases, asystole.[35-40] Failure to synchronize the shock to the R wave may result in ventricular fibrillation.[36,41] Electrical cardioversion generally carries a high success rate (approaching 90%), but, in patients with AMI, there is a substantial risk that the arrhythmia will recur shortly after sinus rhythm is achieved.[33]

AF with Congestive Heart Failure. Patients with congestive heart failure and rapid AF also pose a management dilemma. A rapid ventricular response decreases ventricular filling and compromises cardiac output. The irregularity of the arrhythmia further decreases ventricular contractility and cardiac output.[42] If the degree of congestive heart failure is mild to moderate, then rate control with digoxin or diltiazem may suffice. In patients with severe congestive heart failure, there is a risk of symptomatic hypotension with diltiazem,[25] and digoxin is not capable of rapidly slowing the ventricular response. In these high-risk patients, DC cardioversion carries the slight danger of exacerbating heart failure through ventricular stunning, hypotension, or bradyarrhythmias.[43] There is also the problem of recurrence of the arrhythmia after an initially successful cardioversion.[33]

Some newer studies have addressed the use of intravenous amiodarone in hemodynamically destabilizing AF with severely depressed left ventricular function. Amiodarone has relatively little negative inotropy, and, even if sinus rhythm is not restored, control of the ventricular rate may confer substantial hemodynamic improvement.[33,44-47] In these high risk patients, many of whom require vasopressor support, the conversion rate to sinus rhythm is high, and amiodarone is well tolerated. However, there is a small risk of severe bradycardia, exacerbation of heart failure, and death. No consensus has yet emerged concerning the use of amiodarone in this difficult setting. For the time being, physicians should still attempt emergency DC cardioversion for severely compromised patients with heart failure and rapid ventricular rates. Intravenous amiodarone should be reserved for those patients who fail cardioversion.

AF with Hypotension. In general, a rapid ventricular rate does not lead to hypotension, although this tacharrhythmia will cause decreased cardiac output from impaired ventricular filling. Patients with rapid AF and significant hypotension usually have comorbidities that, combined with a rapid ventricular rate, produce hypotension. One should consider the possibility of intravascular volume depletion (from dehydration or blood loss), drug induced arterial dilatation, pulmonary embolism, cardiac tamponade, septic shock, and cardiogenic shock.

Table 4. Vaughn Williams Classification of Drugs Used in Atrial Fibrillation

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

Patients with rapid rates and symptomatic hypotension who are not volume overloaded should receive a fluid challenge. Failure to respond to a fluid challenge mandates emergency cardioversion. Patients who fail to respond to emergency cardioversion, or who revert to AF, will require pressor support and rate control with intravenous amiodarone and digoxin.[47] Calcium channel blockers and beta blockers are strictly contraindicated in the setting of hypotension.

The AF Patient with Preexcitation Syndrome. Wolff-Parkinson-White (WPW) and other accessory pathway syndromes can predispose to AF. When AF occurs in this subgroup of patients, activation of the ventricles may occur via the AV node, the accessory pathway, or, simultaneously, by both pathways. It should be stressed that the accessory pathway may be capable of conduction so as to produce ventricular rates faster than those seen with AV node conduction. Drugs used to slow the ventricular rate, by selectively blocking the AV node, may accelerate conduction through the bypass tract, leading to dramatic increases in rate and hemodynamic compromise. Rapidly conducted AF can degenerate into ventricular fibrillation in WPW patients (especially in those who have multiple accessory pathways).[48] Hence, there is some urgency in managing AF in patients with WPW. Intravenous procainamide slows conduction through the bypass tract and may chemically convert the rhythm to sinus. Stable patients should receive intravenous procainamide. Digoxin, beta blockers, or calcium channel blockers should not be used, since they can lead to preferential conduction through the bypass tract. Hemodynamically unstable patients should be shocked immediately, as should patients who fail to respond to procainamide, and patients with rates above 250 (they are at the highest risk of degeneration to VF).[49]

Thyrotoxicosis and AF. Thyroid disease may have a profound effect on cardiac performance. Thyrotoxicosis is characterized by a hyperdynamic circulatory state, in part due to increased total blood volume, decreased systemic vascular resistance, and a shortened circulation time. Thyroid hormone also acts as a positive chronotrope. In addition, left ventricular contractility is enhanced in thyrotoxicosis, as is left ventricular diastolic relaxation. Stroke volume and cardiac output are increased. One typically encounters a sinus tachycardia with a wide pulse pressure. AF is also common, occurring in 9-22% of patients with thyrotoxicosis.[49] The rapid ventricular response is usually refractory to standard doses of digoxin, but responds well to beta blocker therapy. Stable patients with thyrotoxicosis may be treated with oral beta blockers. The nonselective beta blocker propranolol is the drug of choice. Intravenous beta blocker therapy should be given in the ED for patients who require rapid rate control.

Severe thyrotoxicosis may result in a state of high output congestive heart failure. Although beta blockers are generally contraindicated in heart failure, in this setting beta blockade therapy may lead to rapid and dramatic improvement. Intravenous esmolol is the drug of choice in high-output failure due to thyrotoxicosis. Some patients, however—those who have progressed to an irreversible dilated cardiomyopathy, or may have underlying structural heart disease—will require conventional therapy with diuretics and traditional pre- and afterload reducing agents.

The Young Patient with AF. Although there is some heterogeneity in young (< 35 years) patients with AF, many will have "lone AF." These patients may present with new onset AF, with no apparent cardiac or systemic illnesses to account for the arrhythmia, or they may give a history of recurrent bouts of AF with a prior workup that has revealed no significant pathology. The dilemma is management to determine whether to pursue a rate control strategy or whether to cardiovert. One should base this decision in part upon the patient's history. For example, a patient who has had multiple prior bouts of AF is unlikely to remain in sinus rhythm if cardioverted in the ED, and should be treated with diltiazem to control the ventricular response. Diltiazem is superior to other agents in this setting. Verapamil has a greater potential to lower blood pressure and decrease contractility than diltiazem. Warfarin should not be given if the patient has lone AF since the risk of thromboembolism is extremely low in the absence of anticoagulation. In patients younger than 60 years with lone AF, the risk of thromboembolism is no greater than that of the general population.[50]

A young patient with a first episode of AF should be offered chemical cardioversion with intravenous ibutilide or electrical cardioversion under deep sedation. One should keep in mind that many patients who decline intervention will convert to sinus rhythm spontaneously. In addition, many patients successfully converted to a sinus mechanism (using either ibutilide or electricity) will eventually revert to AF.

Chemical Cardioversion of AF in the ED

Chemical cardioversion of acute AF in the ED has not yet gained widespread use, in part, because of a number of logistic factors. Patients must be carefully selected to minimize the risk of stroke and cardiac complications. Class IA and IC antiarrhythmics have shown moderate efficacy, but have some proarrhythmic and negative inotropic effects, requiring close inpatient monitoring.[51-53] The class III agents, amiodarone and sotolol, have been studied, but conversion rates in some studies have been disappointing, and both drugs require inpatient monitoring. Traditional drugs used to control the ventricular response (digoxin, diltiazem, verapamil, and pure beta blockers) do not reliably convert AF to sinus rhythm.[54] *(See Table 4.)*

Ibutilide is the first practical agent for ED use for chemical cardioversion of patients with new onset AF (< 48 hours). Ibutilide falls into the class III category of antiarrhythmic drugs and has the advantage of intravenous administration and a short half-life, so that within four hours of administration, the drug's electrophysiologic effects (prolongation of repolarization) are completely resolved.[55,56] Unfortunately, conversion rates for patients with AF treated with ibutilide are less than complete, with a reported success rate of about 30-50%.[57]

Table 5. Emergency Electrical Cardioversion

- Choose a short-acting, intravenous anesthetic, or amnestic agent: Propofol, methohexitol, and midazolam are ideal
- Paddle placement: Hand held-right parasternal 2nd, 3d ICS and left lateral at cardiac apexor defibrillator pad-left parasternal and left posterior chest
- Energy: 200 joules initially, if unsuccessful wait 3 minutes, then 300 joules (if still unsuccessful, 360 joules). Synchronization on the R wave will prevent ventricular fibrillation

Table 6. Anticoagulation Guidelines in Atrial Fibrillation

- Recent congestive heart failure, or fractional shortening less than 25%*
- Rheumatic heart disease*
- Prior thromboembolism*
- Female sex, older than 75 years *
- Hypertension: Treat with warfarin or aspirin depending on patient preference and individual risk of complications
- None of the above risk factors: Treat with aspirin, 325 mg/day

* These risk factors require treatment with warfarin

Ibutilide's effects on repolarization increase the risk of polymorphic ventricular tachycardia. Most of these cases terminate spontaneously; however, about 2% of patients treated with ibutilide will have sustained VT that requires electrical cardioversion.[58] Hence, patients should not be treated with ibutilide unless they are also suitable candidates for electrical cardioversion. Prior to giving ibutilide, patients should be in a fasting state; they must have normal electrolytes (incuding serum magnesium); and there should be no prior history of torsade de pointes, ventricular tachycardia, or sick sinus syndrome. Patients should also be excluded from ibutilide therapy if they have slow heart rates not caused by AV node blocking drugs, or if there is congestive heart failure or hypotension.

The greatest impediment to the practice of chemical cardioversion in the ED has to do with disappointing long-term outcomes. Only a small percentage of patients remain in sinus rhythm in the absence of chronic antiarrhythmic therapy. In general, drugs used to maintain sinus rhythm must be started days prior to chemical or electrical cardioversion. *(See Table 5.)* Ongoing clinical trials including Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) and others will eventually determine which is superior: A strategy of rate control or pharmacological maintainance of sinus rhythm.

Prevention of Thromboembolism

The risk of stroke from cardiac emboli in chronic AF is significant; therefore, ED physicians must address the issue of anticoagulation. The Framingham Heart Study showed an overall risk of stroke of 5% per year in patients with nonvalvular AF.[59] The Stoke Prevention in Atrial Fibrillation (SPAF) study showed a stroke risk of 6.2% per year in non-anticoagulated patients.[60] There are important risk factors for stroke in the setting of AF. The presence of structural heart disease (i.e., left ventricular dysfunction, congestive heart failure, valvular heart disease, coronary artery disease, and left atrial enlargement) identifies a high-risk group for thromboembolism.[61,62] Patients with global left ventricular dysfunction have a stroke risk of 12% per year. Systemic factors that increase the risk of stroke are hypertension (5-6%/year), diabetes (8-9%/year), and prior stroke or TIA (12%/year).[61,62]

A number of clinical trials have prospectively evaluated these risk factors to determine which patients benefit from aspirin therapy alone and which require warfarin to achieve a meaningful reduction in stroke risk without an untoward increase in major bleeding complications. Aspirin, when compared with placebo, reduces the risk of stroke by 22%.[63] Warfarin, in contrast, is associated with a 64% reduction in stroke;[63] however, major bleeding can be expected in 2-3% of patients per year who are treated with warfarin.[63]

SPAF III prospectively identified a low-risk group for stroke in nonvalvular AF.[64] Low-risk patients are those with none of the following risk factors: hypertension or history of hypertension, recent congestive heart failure or left ventricular fractional shortening of 25% or less, previous thromboembolism, and female sex at age older than 75 years. Patients with no risk factors may be treated with aspirin (325 mg/day). Patients with hypertension have a moderate risk of stroke. Those patients should receive either aspirin or warfarin depending on the patient's preferences and individual risk of complications from warfarin. Patients with recent congestive heart failure, left ventricular fractional shortening of 25% or less, prior thromboembolism, or female sex older than 75 years have a high (8% per year) risk of stroke and should receive warfarin if there are no contraindications. Care should be taken to keep the INR between 2 and 3, since major bleeding generally occurs when the INR is above 3-3.5.

Numerous studies have demonstrated that 3-4 weeks of anticoagulation prior to attempts at cardioversion decreases the risk of stroke in those patients whose AF has lasted more than 48 hours.[65] *(See Table 6.)* In the absence of anticoagulation, there is a 5-7% risk of stroke. The 3-4 week period of anticoagulation prior to cardioversion reduces the risk of stroke to about 1.2%.[66] An alternative strategy is to perform transesophageal echocardiography in patients with AF of greater than 48 hours duration. In the absence of left atrial thrombus, patients may be safely cardioverted with a risk of stroke equivalent to that in patients receiving four weeks of warfarin prior to cardioversion.[66] Following cardioversion, patients should continue on warfarin for one month because return of atrial contractility may be delayed for several weeks in spite of the presence of p waves on the electrocardiogram.[65,67]

Recognition and Treatment of Thromboemboli in AF

Not all strokes that occur in patients with AF are the result of cardiac emboli. AF patients are a heterogeneous group, many of whom have hypertension, diabetes, atherosclerotic disease, and other conditions that predispose to stroke in the absence of a left atrial thrombus. The use of transesophageal

echocardiography in AF has led to the recognition that some patients have complex plaque in the aortic arch that predisposes to embolic stroke.[68] The diagnosis of a cardioembolic stroke in a patient with AF is presumptive. In general, a cardioembolic etiology is suggested by the following: a) an infarct involving the cerebral surface territory of a single vessel, b) multiple infarcts occurring in different vascular territories, c) evidence of embolization to the extremities or other organs, and d) hemorrhagic infarction.[69]

The emergency physician evaluating a patient with AF and an acute stroke syndrome should perform a noncontrast head CT to exclude the possibility of a hemorrhage. The prothrombin time and INR should be checked. One should not begin immediate anticoagulation with heparin because of the risk of hemorrhagic transformation of the stroke.[70,71] The purpose of later heparinization is not to treat the acute stroke, but rather to prevent further embolic events. The optimal time to initiating anticoagulation following cardioembolic stroke is controversial. Numerous studies have shown a significant incidence in bleeding complications, without improvement in stroke outcome, when heparin is given immediately. There is no need for the emergency physician to immediately begin a heparin infusion. If heparin is started at the time of admission to the hospital, a continuous infusion is given, without a loading dose, in an attempt to minimize the risk of hemorrhagic transformation.

Cardiac emboli may result in acute limb ischemia, presenting with dramatic severe pain, pallor, coldness of the extremity, and a pulse deficit, in which case immediate anticoagulation with heparin (bolus, then continuous infusion) is indicated. Prompt surgical consultation should be obtained. Catheter or operative embolectomy, or infusion of a fibrinolytic agent is performed to restore perfusion to the ischemic limb. Similarly, sudden thromboembolism to a mesenteric artery will produce bowel ischemia and rapid subsequent infarction requiring immediate operative exploration, thrombectomy, and resection of nonviable bowel with primary anastamosis or a diversion.

Disposition

Because AF, is oftentimes not an ischemia-mediated arrhythmia, not all patients with new onset AF require hospitalization to rule out myocardial infarction.[72] Physicians should base the decision to rule out MI based on the presence of angina or anginal equivalents, features of the electrocardiogram, as well as the patient's general risk for having underlying coronary artery disease. In addition to the possibility of ischemia, there are other compelling reasons to admit patients with new onset AF to the hospital. The presence of decompensated heart failure, myocardial contusion, infective endocarditis, hypotension, syncope, renal failure, pneumonia, stroke, or sepsis are all reasonable indications for admission. Many patients with AF are elderly and have substantial comorbidities, including unsuspected conduction system disease that may lead to excessive bradycardia when drugs are given for rate control.

Some patients with new onset AF will spontaneously convert to sinus rhythm in the ED and may be safely discharged home with appropriate follow-up. Of those patients in whom AF persists, it is usually desirable to achieve restoration of sinus rhythm as soon as possible in order to relieve symptoms, prevent electrical remodeling, and to avoid the need for long-term anticoagulation.[73,74] Hence, one can also justify hospitalization of stable patients with new onset AF if they are likely to undergo attempts at chemical or electrical cardioversion.

Summary

ED evaluation and management of patients with AF is not always straightforward. A number of key points should be kept in mind. Drug therapy to control rate can result in significant side effects, including excessive bradycardia, hypotension, and exacerbation of left ventricular dysfunction. The selection of an agent to control rate should be based upon its side effect profile and the urgency surrounding the patient's symptoms and hemodynamic status. Patients who remain in AF are at significant risk for embolic stroke and will require initiation of appropriate anticoagulation. Finally, the decision to admit to the hospital will depend on the degree of cardiovascular instability, the presence of comorbidities, and the patient's suitability for chemical or electrical cardioversion.

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CME Questions

73. Which of the following statements concerning the epidemiology of atrial fibrillation is correct?
    A. Atrial fibrillation is an uncommon arrhythmia.
    B. The prevalence of atrial fibrillation increases with age.
    C. Atrial fibrillation is usually not associated with coexistant heart or systemic disease.
    D. Atrial fibrillation and stroke are unrelated.

74. Which of the following is *not* a cause of atrial fibrillation?
    A. Thyrotoxicosis
    B. Valvular heart disease
    C. Parasitosis
    D. Hypertensive heart disease

75. Which of the following drugs is contraindicated for rate control in heart failure?
    A. Digoxin
    B. Amiodarone
    C. Propranolol
    D. Diltiazem

76. What is the ideal drug for rate control in thyrotoxicosis?
    A. Digoxin
    B. Beta blocker
    C. Flecainide
    D. Propafenone

77. What is the ideal drug for rapid atrial fibrillation due to an accessory pathway such as Wolff-Parkinson-White?
    A. Digoxin
    B. Diltiazem
    C. Propranolol
    D. Procainamide

78. Which of the following is a contraindication to the use of ibutilide?
    A. Hypomagnesemia
    B. Fasting state
    C. History of SVT
    D. An INR in the range of 2-3

79. What is the most common proarrhythic effect of ibutilide?
    A. Mutifocal atrial tachycardia
    B. Ventricular fibrillation
    C. Asystole
    D. Polymorphic ventricular tachycardia

80. Which of the following statements concerning hospitalization of patients with new onset atrial fibrillation is correct?
    A. All patients must be admitted to rule out myocardial infarction.
    B. Only patients with decompensated heart failure require admission.
    C. Patients may beadmitted for cardiovascular instability or for attempts at cardioversion .
    D. Hospitalization is never indicated.

In Future Issues **Anticoagulation**