Atrial Fibrillation

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Abstract

In 2000, some 2.3 million Americans were affected by atrial fibrillation, and that number is expected to rise as our population ages. Atrial fibrillation is both a reflection of active physiologic stressors on the body and a marker of future cardiac disease progression. The disorganized atrial activity that characterizes atrial fibrillation affects cardiac function, metabolic demand, and quality of life. However, our understanding of the etiology and treatment of this condition continues to advance with the result of recent large-scale clinical trials.

Diabetes, hypertension, congestive heart failure, valvular disease, and myocardial infarction are all risk factors in the development of atrial fibrillation. And the diagnosis confers a five-fold increase in the incidence of stroke. (Patients at increased risk for stroke include those with congestive heart failure, hypertension, age greater than 75, diabetes, and previous stroke.) Anticoagulation is a critical action in most cases of atrial fibrillation, as data show a 68% relative risk reduction of stroke when patients are treated with warfarin. Prior to recent trials, achieving sinus rhythm was thought to invariably improve symptoms, cardiac function, and mortality. The adverse effects of antiarrhythmic medications are now being recognized, and treatment strategies emphasizing ventricular rate control have been recommended in recent clinical practice guidelines. This shift in thinking is influencing both outpatient and emergency department management. Controlling the ventricular rate in atrial fibrillation increases cardiac output, decreases the metabolic demand of the heart, and avoids the potentially dangerous side effects of rhythm-control drugs. Rate-control agents should be selected based on the clinical profile of individual patients. A well-chosen subset of patients may benefit from either chemical or electrical cardioversion; this appears to be a reasonably safe procedure and can be accomplished on an outpatient basis.

Understanding causal etiologies, managing risk for stroke (and need for anticoagulation), addressing rate, and assessing the risks of cardioversion are key elements in a comprehensive approach to atrial fibrillation.

Key Words: Fibrillation, atrial; arrhythmia.

Introduction

ATRIAL FIBRILLATION (AF) is the most common arrhythmia in the adult population (1). The presence of atrial fibrillation may be a reflection of active physiologic stressors on the body, as well as a direct influence on future disease progression. The disorganized atrial activity itself affects cardiac function, metabolic demand, and quality of life. Conceptually, AF should be thought of as both a signal of underlying disease and a condition per se unto itself.

The presentation and management of AF will vary according to the setting and circumstances in which it is encountered. The emergency physician may face a patient *in extremis*, hypotensive and unresponsive, clearly requiring rapid evaluation and treatment of the arrhythmia. The internist may have difficult questions regarding the risks and benefits of taking warfarin daily. In both cases, the provider must be aware that decisions made today can have immediate consequences, including clinical deterioration or embolic stroke. Long-term effects, such as atrial remodeling, may also be determined by choices made in the clinic or emergency department (ED). Furthermore, recent evidence has led to revision or reversal of many previously held beliefs regarding how best to manage AF. This article will review the short-term and long-term strategies in managing this widespread condition.

Epidemiology

In 2000, it was estimated that 2.3 million Americans were affected by AF, and the number is expected to more than double over the next fifty years as our population ages (2). Data from the Framingham cohort show a lifetime risk of developing AF of one in four for adults over age 40 (1). Adjusting for co-morbidities within this cohort, the presence of the arrhythmia itself confers an independent relative risk of death of 1.5 and 1.9 for men and women, respectively (3). One of the most debilitating consequences of the disease is the accompanying risk of stroke, which occurs in an es-

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timated 60,000 patients with AF per year (2). Aside from an increase in morbidity and mortality, patients with AF often experience changes in their quality of life owing to symptoms such as palpitations and decreased exercise tolerance (4, 5). The scope of these challenges will grow as our population ages and our understanding of the disease expands.

Etiology / Pathophysiology

When the atria are in fibrillation, contraction occurs at rates of 350 – 900 per minute. The AV node may conduct these impulses to the ventricles at 90 – 170 beats per minute, and often higher. There are several complementary and competing theories regarding the pathophysiology of AF initiation and propagation. AF may be triggered by a premature atrial beat, with the pulmonary vein shown to be a frequent source of ectopy (6, 7). Atrial flutter has also been shown to trigger AF (8). The maintenance of the arrhythmia is classically described using a model of multiple wandering reentry wavelets propagating through atrial myocardium (9, 10). Multiple fronts of excitation colliding within the atrial tissue extinguish or augment one another. The wavelet collisions result in chaotic re-excitation throughout the atria. These re-entry phenomena can occur at rates exceeding the response capability of the myocardium, resulting in fibrillation (8). As this pattern of diffuse re-excitation continues over the course of time, it is believed that both electrophysiologic and structural remodeling of the atria occurs. This remodeling creates a milieu for the arrhythmia to persist—hence the expression "atrial fibrillation begets atrial fibrillation." Paroxysmal AF thus proceeds to persistent (that is, continuous but potentially convertible) AF and onward to permanent AF, refractory to antiarrhythmic efforts.

The disease states that predispose patients to AF have been well studied. Benjamin and coauthors demonstrated diabetes, hypertension, congestive heart failure, valvular disease, and myocardial infarction to be risk factors in its development (11). Over 8% of patients newly diagnosed with clinical hyperthyroidism are also found to be in AF or flutter (12). One study showed a correlation between alcohol consumption and AF (13), but others have failed to show any correlation or have demonstrated a protective effect with imbibing (14); this relationship therefore continues to be an open question. Echocardiography indicated increased left atrial size to be a structural predisposition in the subsequent development of AF (14 – 16).

As mentioned, the presence of AF has prognostic significance for the patient. Its presence is reported to confer up to a five-fold increase in the incidence of stroke, with the cumulative risk averaging out to approximately 5% per year (17). Furthermore, an ischemic stroke in the presence of AF is almost twice as likely to be fatal than strokes occurring in sinus rhythm (18). AF influences further cardiac disease progression through its contribution to development of congestive heart failure. The loss of "atrial kick" from the arrhythmia decreases stroke volume by as much as 20% (19). Tachycardia-related cardiomyopathy in patients with poor rate control may further depress cardiac reserve (20). The presence of AF together with congestive heart failure increases mortality and hospitalization rates compared to heart failure patients in sinus rhythm (21). The relationship between AF and congestive heart failure highlights the broader question of whether AF is an active participant or a passive marker of overall cardiac disease progression.

Atrial Fibrillation and Risk of Stroke

Stroke risk in AF varies across a range of ages and cardiovascular co-morbidities. Therefore, risk-stratification tools have been developed to determine which patients should be considered for anticoagulation. One method used for identifying patients at higher or lower risk for stroke is the $CHADS_2$ risk index (**C**ongestive heart failure, **H**ypertension, **A**ge ≥ 75, **D**iabetes, and **S**troke or transient ischemic attack history) (22), which is an amalgamation of the conclusions from two studies, the Stroke Prevention in Atrial Fibrillation study, and the Atrial Fibrillation Investigators study (18, 23). The authors used clinical features to determine the patient's risk of stroke, with double weight given to a history of previous stroke (Table 1). A $CHADS_2$ score of 0 correlates with an adjusted stroke rate of 1.9 per 100 patient-years; a score of 6 predicts a stroke rate of 18.2 per 100 patient-years. The $CHADS_2$ index was shown to estimate stroke risk more completely than either of the other two

TABLE 1
$CHADS_2$ Clinical Classification Scheme for Predicting Stroke (22)

Stroke Risk Factor	Score
Congestive Heart Failure	1
Hypertension	1
Age ≥ 75	1
Diabetes Mellitus	1
Stroke History	2
	6

classification schemes alone. $CHADS_2$ has recently been shown to be more robust compared to other stratification schemes, but other decision rules have been proposed (24–26). Ideally, these risk stratification schemes allow the clinician to individualize therapeutic choices by balancing the patient's risk of developing a stroke with the risks and benefits of specific anticoagulation agents. As an example, certain patients may be appropriate candidates for more conservative anticoagulation strategies, such as using aspirin alone (27).

Chemical assays may soon play a role in stroke risk stratification. C-reactive protein is being investigated as a marker of inflammatory burden in certain chronic conditions, including coronary artery disease and stroke (28). It has been found to be elevated in patients experiencing new-onset arrhythmias during the immediate post-cardiopulmonary bypass period (29, 30). In the future, levels of this substance may assist in determining stroke risk in patients with AF (31).

Diagnosis

Electrocardiographic manifestations of AF include irregularly irregular R-R intervals, absence of P waves, and fibrillatory waves of varying morphology. These F waves are best seen in leads V1, II, III, and aVF (32). Although the diagnosis of AF is straightforward in most cases, the practitioner should be aware of potential pitfalls. The patient with an electronically paced rhythm, digoxin toxicity, or heart block may have regular R-R intervals. This regularity may lead to the false conclusion that an atrial arrhythmia is absent, causing the clinician to overlook a potentially catastrophic condition. Multifocal atrial tachycardia and wandering atrial pacemaker can both have irregular ventricular responses; careful attention to the presence of P waves of differing morphology will elucidate their true identity. Likewise, rapid ventricular response can make visualizing the P waves difficult. One strategy that may be used in this setting is to increase the speed of the electrocardiogram (ECG) rhythm strip, to better visualize fibrillation waves (33). Another approach, when the diagnosis continues to be unclear, is a trial of adenosine. During the transient blockade of the AV node, the underlying rhythm can often be appreciated. Even though adenosine appears to be safe for this indication, caution should be exercised when using it in the setting of possible accessory pathways, specifically in an irregular wide-complex tachycardia (34).

Recognition of AF mandates investigation into its etiology, its previous course, and likely outcome. A complete history and a previous ECG will help determine if the arrhythmia is new-onset or chronic. Risk factors for stroke and bleeding will guide the risk/benefit analysis of using anticoagulation. As mentioned previously, AF can be a signal for the presence of underlying pathology, and the history and physical exam will focus the search for an underlying cause of the rhythm change. With new-onset AF, one should consider pulmonary embolism, cardiac ischemia, congestive heart failure, "holiday heart" (due to arrhythmogenicity in binge ethanol consumption), increased vagal tone (35), and hyperthyroidism, among many possibilities (Table 2). Even after a thorough workup, 30% or more of chronic AF remains idiopathic (36). To determine why a patient's chronic AF has a rapid ventricular response, consider conditions that may increase sympathetic tone or work directly on the AV node: fever, dehydration, gastrointestinal (GI) bleed, sepsis, medication noncompliance, and many more.

Treatment

Treatment of AF is directed by the following factors:

(1) patient stability
(2) underlying etiology of arrhythmia
(3) symptoms
(4) ventricular rate
(5) risk factors for stroke

The first step in caring for AF is to recognize a critically ill patient and rapidly address the unstable rhythm. The Advanced Cardiac Life Support (ACLS) guidelines from the American Heart Association state that the provider must be prepared for immediate cardioversion with any ventricular rate over 150, and should take action as the clinical picture dictates (37). Pre-medication of the patient prior to any shock delivery with sedatives and analgesia is ideal, but the provider must take into consideration the patient's physiologic reserve and ability to tolerate the medication. The sequence of synchronized cardioversion using monophasic waveforms proceeds starting at 100J (50J for atrial flutter), increasing to 200J, 300J, and finally 360J.

TABLE 2
Causes of Atrial Fibrillation

Alcohol intake	Ischemia/Infarction
Congestive heart failure	Medications
Electrocution	Myocarditis
Electrolyte abnormalities	Pericarditis
Hypertension	Pulmonary embolism
Hyperthyroidism	Surgery
Idiopathic	Valvular heart disease
Increased sympathetic states	
Gastrointestinal bleed	
Hypovolemia	

One study of 64 patients suggested that an energy level of 100J is too low to convert most patients, and recommended starting at 200J (38). Biphasic devices deliver current at a lower energy level, and have device-specific recommendations. Recognize that instability applies to both vital signs and the overall clinical status: pulmonary congestion, altered mental status, and severe chest pain are typically considered signs of decompensation. As discussed above, the physician must recognize and address any underlying physiologic imbalances that may have precipitated the arrhythmia. Exploring possibilities such as infection, a pulmonary process or intravascular volume loss will prevent a false sense of security from delaying definitive treatment.

Rate or Rhythm: Which Strategy Is Best?

Prior to several recent large trials, it was assumed (but unproven) that patients with persistent AF received benefit from aggressive treatment to maintain a sinus rhythm. Intuitively, maintaining sinus rhythm would seem preferable for the sake of improved cardiac function and symptom control. However, investigators began to suspect that the adverse effects of antiarrhythmic medications might weigh against the overall benefit of this treatment strategy (39). In contrast, an approach focused on maintaining a lower heart rate, along with adequate anticoagulation, might be a preferable alternative.

The landmark AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) trial enrolled 4,060 patients with AF and risk factors for stroke or death (40). Patients were randomized into rhythm- or rate-control groups. The investigators found no difference between the two groups in death or composite morbidity; an increase in subsequent hospitalization rates was found in the rhythm control group (80.1% vs. 73%). Most surprisingly, the strategy of maintaining sinus rhythm did not lower the rate of ischemic stroke over rate-controlled patients. The authors concluded that controlling the ventricular rate, along with anticoagulation, was at least as effective in preventing morbidity and mortality in patients with AF as traditional antiarrhythmic strategies (41, 42). This outcome equivalence between the two strategies was also established in the European RACE trial of 522 patients (43), and subsequent studies (44). Focusing on rate rather than rhythm has also been shown to be more cost-effective (45, 46).

The AFFIRM data demonstrate that patients presumed to be maintained in sinus rhythm have stroke rates similar to those patients in rate-controlled AF. Possible explanations of this finding include medication inefficacy, non-compliance, or undetected paroxysms of AF with thrombus formation in patients believed to always be in sinus rhythm. This last point is supported by a recent study of patients with implanted pacemakers who were maintained on antiarrhythmic medications and who demonstrated a significant number of asymptomatic episodes of AF, some lasting greater than 24 hours (47). It follows that freedom from symptoms in patients with known paroxysmal or permanent AF may not be a guarantee against thrombus formation. This may be especially true in patients using rate-lowering agents, so that ventricular response may be moderately suppressed, obscuring recognition of the exact moment the arrhythmia began. In any ambiguous situation, a cardioversion plan without adequate anticoagulation should be carefully scrutinized.

The evidence supporting an outpatient strategy of rate-control with anticoagulation has gained credence since these studies were published, and were incorporated into the clinical guidelines for managing AF by the American College of Physicians. This shift in thinking also relates to emergency physicians who may be inclined to aggressively cardiovert stable patients in AF; the benefits of acute rhythm control may not balance the risks of the procedure.

Rhythm Strategies

There are certain circumstances where the physician may consider elective cardioversion (either chemical or electrical). Symptoms affecting quality of life, younger patients with a lower risk of thromboembolism, or patient preference may all be reasons to attempt cardioversion. Failure of rate control measures or contraindications to anticoagulation may also push the clinician towards sinus rhythm maintenance. Before embarking on this approach, however, the risks associated with cardioversion should be evaluated. The physician must assess the possibility of thrombus in the fibrillating atria, which may dislodge upon reversion to sinus rhythm, a risk estimated to be less than 1% over eight weeks following cardioversion (48). The traditional teaching has been that patients in fibrillation for less than 48 hours have a low risk of thrombus formation. But, the risk is not zero, and one study has shown echocardiographic evidence of thrombus in the left atrial appendage less than three days after the arrhythmia begins (40). As mentioned above, patient history may not be a reliable indicator for the absence of AF in the recent past.

The procedure for electrical cardioversion is carried out in a similar fashion to that of the unstable patient, except it occurs in a controlled environment with judicious use of sedation. In one multicenter-ED-based trial of 388 patients, electrical cardioversion in a low-risk cohort had an 86% success rate, with few complications from the procedure. In this study, long-term follow-up assessing thromboembolism occurrence was not performed, and further investigation into the safety of this strategy should be conducted (49).

With chemical cardioversion, there are several approved agents to choose from. In a meta-analysis conducted during their guideline development, the American College of Physicians found that ibutilide, flecainide, dofetilide, propafenone, and amiodarone all had strong evidence supporting their safety and efficacy, with ibutilide having an odds ratio of conversion equal to 30.7:1 over placebo (50). Table 3 details dosing and side effects for commonly used cardioversion agents. The chemically cardioverted patient must be observed after the procedure for subsequent medication-induced arrhythmias, such as *torsades de pointes*. Given these considerations, along with the moderate failure rate of the procedure (10 – 30%) and a high chance of recurrence, the candidates for elective cardioversion of AF must be thoroughly educated regarding the risks and benefits of this procedure before making a decision (51 – 53).

Immediately following electrical or chemical cardioversion, there is a period of "atrial stunning," a stasis environment that may predispose to thrombus formation for up to two weeks following the procedure (54). The American Academy of Family Physicians/American College of Cardiology (AAFP/ACP) guidelines recommend three weeks of anticoagulation prior to cardioversion, followed by four weeks of anticoagulation in order to avoid these risks. An alternate strategy recommended is evaluation by trans-esophageal echocardiography, followed by three weeks of anticoagulation during the period of atrial stunning (see "Guidelines" section below).

Rate-Control Agents

Controlling the ventricular rate in AF increases cardiac output, decreases the metabolic demand of the heart, and avoids the potentially dangerous side effects of rhythm-control drugs. The selection of a medication to control rate, either in the ED or for the outpatient, should be made in light of the clinical circumstances. Each agent also has the potential to spontaneously convert the patient back to a sinus rhythm, so risk-stratification for thromboembolic disease should be performed before choosing a drug.

Nondihydropyridine calcium channel antagonists are commonly used rate agents. They are active at the AV node and relatively safe, and have a

TABLE 3
Medications for Cardioversion of Atrial Fibrillation to Sinus Rhythm

Drug	Dosage	Route	OR of conversion over placebo	Side Effects
Ibutilide	1 mg over 10 min	IV	30.7	QT prolongation, *torsade de pointes*
Flecainide	200 – 300 mg PO/ 1.5 – 3.0 mg/kg IV over 10 – 20 min	Oral/IV	13.2	Hypotension, rapid atrial flutter
Propafenone	450 – 600 mg PO/ 1.5 – 2.0 mg/kg over 20 min	Oral/IV	3.9	Hypotension, rapid atrial flutter
Amiodarone	1.2 – 1.8 g/day oral divided until 10g total 5 – 7 mg/kg IV over 60 min, then 1.2 – 1.8 g/day IV infusion until 10 grams	Oral/IV	3.2	Hypotension, bradycardia, QT prolongation, *torsade de pointes*, GI complaints
Dofetilide	Renal dosing	Oral	6.7	QT prolongation, *torsade de pointes*

OR = Odds ratio

demonstrated efficacy in decreasing ventricular rate in comparison to other agents. Diltiazem and verapamil are the agents most commonly used. There may be apprehension about giving a calcium channel blocker in the setting of decompensated heart failure, as the risks of hypotension are thought to be compounded in patients with compromised cardiac function. There have been several studies which have not shown this assumed effect; improvement of stroke volume with increased diastolic filling time may be a reason why further clinical deterioration tends not to occur (55–57). The use of diltiazem rather than verapamil may decrease the incidence of hypotension (58). Another strategy advocated is "priming" the patient with intravenous calcium prior to administration of the calcium channel blocker. By first infusing calcium, the peripheral vasodilatory effects of the calcium channel blocker may be attenuated without affecting AV nodal activity (59–61). This pretreatment effect has been shown in trials using verapamil, but its use with diltiazem has yet to show a significant benefit (62). A dose of 3 mL of calcium chloride or 5 mL of calcium gluconate is recommended.

In the patient with rapid AF presenting with potential myocardial ischemia, a beta blocker is an excellent choice. It is an effective agent for rate control and has mortality benefit in the setting of acute coronary syndrome. A short-acting drug, such as esmolol, can be titrated if hypotension is a concern. Thyrotoxicosis, while not often diagnosed in the emergency department, is another condition for which a beta blocker may be beneficial. Propranolol is considered a first-line agent because of its effects on rate and blood pressure, as well as its activity in blocking peripheral conversion of T_4 to T_3. Always consider contraindications (e.g., bronchospasm) before using a beta blocker.

Caution must be used when using a calcium channel blocker and a beta blocker simultaneously (63). Hypotension, bradyarrhythmias, and AV nodal conductions disturbances have been reported in patients on oral formulations (64). The combined negative chronotropic effects of the medications are further enhanced by reciprocal inhibition of their hepatic clearance (65, 66). This negative synergistic effect may put the acute patient at risk for heart block if the two classes of medications are used concomitantly, especially in elderly patients with left ventricular dysfunction.

Digoxin has historically been used as a rate-controlling agent, especially in heart failure where its inotropic effects could be maximized. Despite this theoretical advantage, its usefulness in the acute setting is limited. Peak rate control effects may not be seen for hours after loading the drug. If there is an increase in the patient's sympathetic drive (often the case in the setting of hypovolemia, cardiac ischemia, or infection), the drug's vagotonic mechanism of AV nodal action will be ineffective (67). Given its significant side effect profile, digoxin should be considered at most a second-line agent for rate control (68).

Amiodarone, a medication approved for treatment of ventricular arrhythmias, has effective beta-blocking properties and has been shown to rapidly control rate in the new-onset AF patient (69). Current ACLS guidelines recommend amiodarone for rate control of AF in stable patients with known ejection fractions of less than 40% (70). Additionally, amiodarone may be preferable to calcium channel blockers when adequate blood pressure is a concern. In a study of 60 intensive care unit patients in rapid AF, amiodarone was shown less likely to cause hypotension than diltiazem (although the calcium channel blocker was superior in controlling ventricular rate at 24 hours (71). Amiodarone is also useful in the setting of a wide-complex tachycardia of uncertain origin, where the drug's antiarrhythmic properties are active against both ventricular and supraventricular sources (72). A previous drawback to its use was perceived expense; generic formulations of amiodarone have recently become available and may reduce this cost.

Magnesium has also been shown to be effective at rate control in AF. When given as bolus followed by infusion, it was shown to have rate-control effects comparable to those of amiodarone, and significantly higher rates of reversion to sinus rhythm than diltiazem (57% vs. 22%) (73, 74). Magnesium's efficacy and low cost make it an attractive rate-control option.

When giving any rate-control agent, it is important to consider the potential to convert the rhythm back to sinus—a dangerous occurrence in patients unprotected from embolic stroke (75). Although the cessation of AF may be unrelated to the medication, it is clear that these agents can cause reversion to a sinus rhythm. The conversion risk for each drug is difficult to estimate, but the clinician is still advised to consider this effect when rate-controlling a patient not on anticoagulation (Table 4).

In cases of AF refractory to pharmacologic rate control, AV nodal ablation and permanent pacemaker placement may be required for definitive rate control.

Anticoagulation

Since the advent of electrical cardioversion by Lown in the 1960s (76–78), it was recognized that

TABLE 4
Rate-Control Medications for Atrial Fibrillation with Rapid Ventricular Response

Drug	Loading Dose	Maintenance Dose	Onset	Side Effects	Patient Population	Conversion Rate Acute	Remarks
Diltiazem	0.25 mg/kg IV over 2 min	5 – 15 mg/hr	2 – 7 min	Hypotension, decreased AV nodal conduction	Stable patients	50 – 66%	Can "prime" with calcium to prevent hypotension
Metoprolol	2.5 – 5 mg IV bolus over 2 min up to 3 doses	N/A	5 min	Hypotension, AV nodal conduction disturbances, bronchospasm	Ischemia, thyrotoxicosis	57%	Avoid using together with CCB
Esmolol	0.5 mg/kg over 1 min	0.05 –0.2 mg/kg/min	5 min	Hypotension, AV nodal conduction disturbances, bronchospasm	Ischemia, thyrotoxicosis	80%	Easy to titrate in patients with border-line BP
Magnesium	1 gram over 20 min	Variable	5 min	Hypotension	Mg-depleted (i.e., alcoholics)	60 – 78%	Inexpensive
Amiodarone	150 mg IV bolus over 10 min	1 mg/min for 6 h, then 0.5 mg/min for 18 h	20 min	Hypotension	Wide complex tachycardia, borderline BP	43 – 80%	Newer generic formulations available. Not approved for supra-ventricular arrhythmias
Digoxin	0.25 mg IV every 2 hours up to 1.5 mg	N/A	2 hours	Digoxin toxicity, heart block	Refractory to first-line therapy	Similar to placebo	Not recom-mended as first-line agent

CCB = calcium channel blockers; Mg = magnesium.

anticoagulation prevented embolic events after the procedure (79, 80). Data pooled from multiple studies show a relative risk reduction for stroke of 68% in patients treated with warfarin (an absolute risk reduction of 3.1%) (81). In the AFFIRM trial experience, it was found that most patients with stroke and AF had either sub-therapeutic anticoagulation or had discontinued their anticoagulation medications altogether. Recent trials have examined the use of a combination strategy of employing lower levels of anticoagulation combined with antiplatelet agents, and the results show an encouraging trend towards better outcomes and fewer side effects (specifically vascular death, transient ischemic attack, and nonfatal stroke or systemic embolism) (82). This strategy may become more widespread in the near future, pending results of investigations into bleeding rates with antiplatelet and anticoagulant combination therapy (83, 84). As emphasized above, it is critical that the physician identify patients at high risk for stroke to formulate an anticoagulation strategy.

While not officially approved for anticoagulation in the setting of AF, the use of low-molecular-weight-heparin (LMWH) has been investigated as a bridge to outpatient oral anticoagulation (85, 86). One small study of 18 patients showed a trend towards decreased cost and length of stay when LMWH was used in an ED-based cardioversion strategy (87), and another study suggests that using LMWH may shorten recommended anticoagulation times prior to cardioversion (88). As the indications for these versatile drugs continue to expand, we can expect more data on this topic in the future.

Pearls and Pitfalls

- Diltiazem can be safe for patients with LV dysfunction. Consider pre-treatment with calcium to avoid hypotension.
- Avoid using beta blockers and calcium channel blockers simultaneously in the same patient.
- Consider digoxin a second-line agent in cases refractory to calcium channel or beta blockade.
- Keep in mind the intrinsic ability of some rate-controlling agents to convert the arrhythmia back to sinus—and be prepared for the consequences.
- If the patient is taking digoxin, cardioversion may inadvertently lead to heart block.
- Patient history may not always be a reliable indicator of the initiation of atrial fibrillation.

Key Concepts

- The presence of atrial fibrillation or a rapid ventricular rate may be a sign of an extra-cardiac physiologic disturbance (ischemia, GI bleed, pulmonary embolism, hypothermia, electrolyte disturbances).
- Risk-stratifying patients using a clinical decision tool such as $CHADS_2$ is helpful in assessing the benefit of chronic anticoagulation.
- Rate-control agents may yield additional benefit in certain situations, such as cardiac ischemia and hypotension.
- Before cardioverting a patient in the emergency department, weigh both the long- and short-term benefits against the risks of embolic stroke and other complications.

There are emerging alternative options to traditional anticoagulation agents that may be of use in the coming years. A new class of medication, direct thrombin inhibitors, has been investigated in industry-sponsored European trials (89). The studies have shown their equivalency to warfarin in prevention of stroke in AF patients. The advantage of this medication (ximelagatran) is that it is administered in a fixed dose, with no need for frequent coagulation monitoring. Although available in some European markets, it is not currently approved for use in the United States.

A new device, PLAATO® (ev3 Inc., Plymouth, MN), is positioned by a catheter into the left atrial appendage, theoretically preventing thrombus from forming. It is not known if this device could preclude the use of anticoagulants in patients at risk for thromboembolic disease.

Treatment Guidelines

Groups involved in creating guidelines for the treatment of AF include the American College of Cardiology, American Academy of Family Physicians, American College of Physicians, and American College of Chest Surgeons. The most recent guidelines, formulated by a joint panel of the ACP and AAFP, make the following recommendations (50) (with the associated evidence grades in parentheses):

- Rate control with chronic anticoagulation is the recommended strategy for most atrial fibrillation patients (Grade 2A)
- Use warfarin unless patients are in a low-risk group or have contraindications for its use (Grade 1A)
- Atenolol, metoprolol, diltiazem and verapamil are recommended for rate control as an outpatient; digoxin should be considered second-line therapy for patients who do not exercise (Grade 1B)
- For patients opting for cardioversion, direct current (Grade 1C+) or pharmacologic conversion (Grade 2A) are both appropriate options.

- Either transesophageal echocardiogram (TEE) with early cardioversion, or three weeks of anticoagulation prior to cardioversion, are acceptable strategies to minimize stroke risk in patients electing cardioversion. Both strategies are followed by three to four weeks of anticoagulation (Grade 2A)
- Antiarrhythmic medications are generally not recommended, as risks likely outweigh benefits (Grade 2A)

Since more research is being conducted on management strategies for atrial fibrillation, clinical policies from other professional bodies may be forthcoming, helping to synthesize the vast amount of literature on the topic.

Conclusion

As the incidence of atrial fibrillation increases and our therapeutic options continue to expand, the primary care physician must think a step beyond the urgent clinical issues at the bedside when a patient presents with the disease. He or she must recognize the underlying pathophysiology that the arrhythmia is built upon, as well as the potential acute and long-term hemodynamic and neurological consequences of not employing a comprehensive strategy. Pursuing root causes, managing risk for stroke, addressing rate, and weighing the risks of cardioversion form a framework for developing such a strategy.

Practice Guidelines

"Management of Newly Detected Atrial Fibrillation: A Clinical Practice Guideline from the American Academy of Family Physicians and the American College of Physicians"—2003 (50)

"ACC/AHA/ESC Guidelines for the Management of Patients with Atrial Fibrillation"—2001 (32)

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