Management of Newly Detected Atrial Fibrillation: A Clinical Practice Guideline from the American Academy of Family Physicians and the American College of Physicians

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The Joint Panel of the American Academy of Family Physicians and the American College of Physicians, in collaboration with the Johns Hopkins Evidence-based Practice Center, systematically reviewed the available evidence on the management of newly detected atrial fibrillation and developed recommendations for adult patients with first-detected atrial fibrillation. The recommendations do not apply to patients with postoperative or post–myocardial infarction atrial fibrillation, patients with class IV heart failure, patients already taking antiarrhythmic drugs, or patients with valvular disease. The target physician audience is internists and family physicians dedicated to primary care. The recommendations are as follows:

Recommendation 1: Rate control with chronic anticoagulation is the recommended strategy for the majority of patients with atrial fibrillation. Rhythm control has not been shown to be superior to rate control (with chronic anticoagulation) in reducing morbidity and mortality and may be inferior in some patient subgroups to rate control. Rhythm control is appropriate when based on other special considerations, such as patient symptoms, exercise tolerance, and patient preference. **Grade: 2A**

Recommendation 2: Patients with atrial fibrillation should receive chronic anticoagulation with adjusted-dose warfarin, unless they are at low risk of stroke or have a specific contraindication to the use of warfarin (thrombocytopenia, recent trauma or surgery, alcoholism). **Grade: 1A**

Recommendation 3: For patients with atrial fibrillation, the following drugs are recommended for their demonstrated efficacy in rate control during exercise and while at rest: atenolol, metoprolol, diltiazem, and verapamil (drugs listed alphabetically by class). Digoxin is only effective for rate control at rest and therefore should only be used as a second-line agent for rate control in atrial fibrillation. **Grade: 1B**

Recommendation 4: For those patients who elect to undergo acute cardioversion to achieve sinus rhythm in atrial fibrillation, both direct-current cardioversion **(Grade: 1C+)** ***and pharmacological conversion*** **(Grade: 2A)** ***are appropriate options.***

Recommendation 5: Both transesophageal echocardiography with short-term prior anticoagulation followed by early acute cardioversion (in the absence of intracardiac thrombus) with postcardioversion anticoagulation versus delayed cardioversion with pre- and postanticoagulation are appropriate management strategies for those patients who elect to undergo cardioversion. **Grade: 2A**

Recommendation 6: Most patients converted to sinus rhythm from atrial fibrillation should not be placed on rhythm maintenance therapy since the risks outweigh the benefits. In a selected group of patients whose quality of life is compromised by atrial fibrillation, the recommended pharmacologic agents for rhythm maintenance are amiodarone, disopyramide, propafenone, and sotalol (drugs listed in alphabetical order). The choice of agent predominantly depends on specific risk of side effects based on patient characteristics. **Grade: 2A**

Ann Intern Med. 2003;139:1009-1017. **www.annals.org**

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See related article on pp 1018-1033.

Atrial fibrillation is the most common type of arrhythmia in adults. It is more common as patients age; the prevalence is 1% among those younger than age 60 years and increases to more than 8% in those older than age 80 years. When data are adjusted for age, men are affected more often than women. Cardiac conditions associated with the development of atrial fibrillation are hypertension, rheumatic mitral valve disease, coronary artery disease, and congestive heart failure. Noncardiac causes include hyperthyroidism, hypoxic pulmonary conditions, surgery, and alcohol intoxication. Patients with atrial fibrillation may have symptoms of hemodynamic compromise, such as irregular palpitations and lightheadedness, or more vague symptoms, such as malaise, but may be asymptomatic. Patients with atrial fibrillation are at increased risk for thromboembolic disease.

The purpose of this guideline is to make recommendations on the pharmacologic management of newly detected atrial fibrillation in primary care. The target patient population is adult patients with first-detected atrial fibrillation, defined as the presence of symptoms or electrocardiographic evidence of atrial fibrillation. The American College of Cardiology/American Heart Association has recommended using first-detected atrial fibrillation regardless of whether it is symptomatic or self-limited, recognizing that there can be uncertainty about the duration of the episode and about previous undetected episodes (1). This guideline does not apply to patients with postoperative or post–myocardial infarction atrial fibrillation, patients with class IV heart failure, patients already taking antiarrhythmic drugs, or patients with valvular disease. The target physician audience is internists and family physicians dedicated to primary care.

This guideline is based on the accompanying background paper by McNamara and colleagues (2) and on the evidence report "Management of New-Onset Atrial Fibrillation" (3), which was produced by the Johns Hopkins Evidence-based Practice Center under contract to the

Table 1. **The Guyatt Approach to Grading Recommendations***

Grade of Recommendation	Clarity of Risk–Benefit	Methodologic Strength of Supporting Evidence	Implications
1A	Clear	Randomized trials without important limitations	Strong recommendation; can apply to most patients in most circumstances without reservation
1B	Clear	Randomized trials without important limitations (inconsistent results, nonfatal methodologic flaws)	Strong recommendation; likely to apply to most patients
1C+	Clear	No randomized trials for this specific patient or patient population, but results from randomized trial(s) including different patients can be unequivocally extrapolated to the patient under current consideration; or overwhelming evidence from observational studies is available	Strong recommendation; can apply to most patients in most circumstances
1C	Clear	Observational studies	Intermediate-strength recommendation; may change when stronger evidence is available
2A	Unclear	Randomized trials without important limitations	Intermediate-strength recommendation; best action may differ depending on circumstances or patients' or societal values
2B	Unclear	Randomized trials without important limitations (inconsistent results, nonfatal methodologic flaws)	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances
2C	Unclear	Observational studies	Very weak recommendation; other alternatives may be equally reasonable

* Adapted from reference 4.

Agency for Healthcare Research and Quality (AHRQ), Rockville, Maryland. The American Academy of Family Physicians (AAFP) and the American College of Physicians (ACP) created this guideline in collaboration. The Joint AAFP/ACP Panel reviewed the evidence and developed and graded the recommendations (**Table 1**). The guideline was then approved by both organizations. The guideline makes recommendations in the following areas: rate control versus rhythm control, stroke prevention and anticoagulation, electrical cardioversion versus pharmacologic cardioversion, the role of transesophageal echocardiography in guiding therapy, and maintenance therapy.

SECTION 1: RATE CONTROL VERSUS RHYTHM CONTROL

One of the fundamental questions in the management of atrial fibrillation is whether to attempt cardioversion. The answer to this question depends on whether rate control or rhythm control provides more effective protection from thromboembolic events, improved mortality, better relief of symptoms, or improved quality of life. Another significant clinical question is whether certain populations, such as women, patients with hypertension or congestive heart failure, or young people with structurally healthy hearts, have better outcomes with one or the other strategy. Four studies have compared rate control with rhythm control. The study samples have generally involved older patients (>65 years of age), and women and younger patients with healthy hearts and paroxysmal atrial fibrillation have not been well represented (5).

The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial compared rhythm control versus rate control, and use of anticoagulation was recommended in both arms (6). More than 4000 patients who were at least 65 years of age or who had at least 1 risk factor for stroke or death, such as hypertension, diabetes, previous stroke, or poor ventricular function, were followed for a mean of 3.5 years. Slightly more than one third of the patients were enrolled after their first episode of atrial fibrillation, and more than 90% had had their qualifying episode within the previous 6 weeks. In more than two thirds of patients, the qualifying episode lasted at least 2 days. The average patient age was 70 years. Sixty-one percent of patients were men, and 89% were white. Seventy-one percent of patients had hypertension, 38% had coronary heart disease, 18% had previously had failure of antiarrhythmic therapy, and 12% had no apparent heart disease (lone atrial fibrillation). Patients were randomly assigned to rate or rhythm control, and their physicians chose the specific therapies (pharmacologic first, then nonpharmacologic if needed). Anticoagulation was continued indefinitely in the rate-control group and was encouraged in the rhythm-control group but could be stopped at the physician's discretion if sinus rhythm had been maintained for at least 4, and preferably 12, consecutive weeks with antiarrhythmic therapy. The prevalence of sinus rhythm in the rhythm-control group was 82%, 73%, and 63% at 1, 3, and 5 years, respectively. The prevalence of sinus rhythm in the rate-control group was 34.6% at 5 years.

The primary end point in the AFFIRM trial, overall mortality, was not statistically significantly different between the groups. However, the rhythm-control strategy was associated with a higher risk for death than the rate-control strategy among older patients, those without congestive heart failure, and those with coronary disease. Rates of stroke also did not differ between groups; 70% of all strokes occurred in patients who had stopped receiving anticoagulation or who had subtherapeutic international nor-

malized ratios (<2.0). More hospitalizations were reported in the rhythm-control group ($P < 0.001$).

Another recent study, the RAte Control versus Electrical cardioversion for persistent atrial fibrillation (RACE) study, randomly assigned patients to receive aggressive rhythm control or rate control (7). This was a smaller study, involving 522 patients (mean age, 68 years). Sixty-four percent of patients were men, 49% had hypertension, and 27% had coronary artery disease. All patients had persistent atrial fibrillation lasting less than 1 year and had had at least 1 previous electrical cardioversion (a maximum of 2 previous cardioversions was permitted for study inclusion). The primary end point was a composite of cardiovascular mortality, heart failure, thromboembolic complications, bleeding, pacemaker implantation, and severe side effects of antiarrhythmic drugs. Again, no difference was seen between groups in the primary composite end point. As in the AFFIRM study, most of the strokes occurred in patients whose anticoagulation had been halted or patients whose international normalized ratio was subtherapeutic (<2.0). In post hoc analysis, a benefit for rate control over rhythm control was seen in patients with hypertension and in women. Since this was a post hoc analysis, these results will need to be confirmed by further studies. Of note, despite an aggressive treatment protocol, at the end of follow-up only 39% of the patients in the rhythm-control group were in sinus rhythm.

The Pharmacological Intervention in Atrial Fibrillation (PIAF) trial randomly assigned 252 patients 18 to 75 years of age with new-onset or permanent symptomatic atrial fibrillation (mean duration of atrial fibrillation, approximately 4 months) to rate control with diltiazem or aggressive conversion (many times if necessary) and maintenance therapy with amiodarone (8). The primary end point of the study was improvement in symptoms related to atrial fibrillation. After 1 year of follow-up, relief of symptoms was similar in both groups, as were quality-of-life measures. Walking distance was improved in the rhythm-control group, but hospital admissions were more frequent in this group.

Although final results are not yet available, preliminary reports of the Strategies of Treatment of Atrial Fibrillation (STAF) trial have been presented (9). Patients were randomly assigned to receive anticoagulation for 3 weeks before conversion and for 4 weeks after attempted conversion, with antiarrhythmic therapy to maintain sinus rhythm, or to long-term anticoagulation and rate control. (Patients included in this study had at least 1 previous conversion attempt.) After more than 1.5 years of follow-up, no difference was seen between the groups in rates of the primary end points of death, stroke, transient ischemic attacks, cardiopulmonary resuscitation, or thromboembolism. Of interest, only 40% of patients in the rhythm-control group were still in sinus rhythm at 1 year, and all primary end points occurred in patients in atrial fibrillation, even in the rhythm-control group. This result has created speculation about whether fewer events would have occurred if anticoagulation had been continued indefinitely in the conversion group. It also suggests that despite aggressive rhythm management, a substantial number of patients cannot maintain sinus rhythm.

In general, the trial samples were older and male and had risk factors for stroke, such as hypertension, congestive heart failure, and coronary disease. Certain subgroups of patients with atrial fibrillation, such as younger patients with healthy hearts or paroxysmal atrial fibrillation, were not well represented in the trials. Therefore, it is not certain whether these subgroups of patients may benefit from more aggressive rhythm control or rate control.

Recommendation 1: Rate control with chronic anticoagulation is the recommended strategy for the majority of patients with atrial fibrillation. Rhythm control has not been shown to be superior to rate control (with chronic anticoagulation) in reducing morbidity and mortality and may be inferior in some patient subgroups to rate control. Rhythm control is appropriate when based on other special considerations, such as patient symptoms, exercise tolerance, and patient preference. Grade: 2A *(Note:* This recommendation received a grade of 2A because of the need to apply the recommendations to different patient populations on the basis of differing patient values and societal issues. The evidence regarding the risk–benefit ratio is clear and of good quality [Grade: 1A].)

Consistent clinical trial data now show that aggressive rhythm control is not superior to rate control in reducing morbidity or mortality and may be inferior in some patient subgroups. Moreover, patients randomly assigned to aggressive rhythm control (with 1 month of anticoagulation postcardioversion) consistently have more hospitalizations and adverse drug events and often do not maintain sinus rhythm. In the AFFIRM trial, there was a trend toward increased mortality in the rhythm-control group for patients who were older than age 65 years, those who did not have congestive heart failure, and those who had coronary heart disease. The RACE trial found a trend for increased mortality in the rhythm-control group in patients with hypertension and in women. The physician and patient must consider these factors, in addition to the patient's symptoms, quality of life, and tolerance for procedures, when making a management decision.

Section 2: Anticoagulation

Sixteen studies that addressed the role of anticoagulation in atrial fibrillation were included in this analysis (10–24). Three of these trials were secondary prevention trials, enrolling patients who had already had a stroke or transient ischemic attack, and thus are analyzed separately (11, 16, 24). Meta-analysis of the primary prevention studies reported on the pooled efficacy (prevention of stroke and peripheral embolism) and safety (major and minor bleeding events) of warfarin versus placebo, aspirin versus placebo, and warfarin versus aspirin. It found that warfarin is more efficacious than placebo for primary stroke preven-

Table 2. **Risk for Stroke Stratified by $CHADS_2$ Score***

$CHADS_2$ Score	Adjusted Stroke Rate (95% CI)	$CHADS_2$ Risk Level
0	1.9 (1.2–3.0)	Low
1	2.8 (2.0–3.8)	Low
2	4.0 (3.1–5.1)	Moderate
3	5.9 (4.6–7.3)	Moderate
4	8.5 (6.3–11.1)	High
5	12.5 (8.2–17.5)	High
6	18.2 (10.5–27.4)	High

* The $CHADS_2$ score is calculated by adding 1 point each for recent congestive heart failure (i.e., active within the past 100 days or documented by echocardiography), hypertension (systolic and/or diastolic), age at least 75 years, and diabetes mellitus, and adding 2 points for a history of stroke or transient ischemic attack. A score of 0 to 1 was designated as low risk; a score of 2 to 3 was designated as moderate risk; and a score of 4, 5, or 6 was designated as high risk. The adjusted stroke ratio is the expected stroke rate per 100 patient-years from the exponential survival model from the National Registry of Atrial Fibrillation.

tion (odds ratio [OR], 0.30 [95% CI, 0.19 to 0.48]), although evidence suggested an increase in major bleeding risk (OR, 1.90 [CI, 0.89 to 4.00]). (The criteria used for the degree of efficacy come from a modification of the original Evidence-based Practice Center report. Strong evidence of efficacy was indicated by an OR $>$ 1.0 and a 99% CI that did not include 1.0 [$P < 0.01$]. Moderate evidence of efficacy was indicated by an OR $>$1.0 and a 95% CI that did not include 1.0 but a 99% CI that did include 1.0 [$0.01 \leq P \leq 0.050$]. Suggestive evidence of efficacy was indicated by a 95% CI that included 1.0 in the lower tail [$0.05 < P < 0.2$]. Inconclusive evidence of efficacy was indicated by a 95% CI that was widely distributed around 1.0. Finally, strong evidence of lack of efficacy was indicated by an OR near 1.0 and a narrow 95% CI.)

The evidence for aspirin versus placebo for primary stroke prevention was suggestive for stroke prevention (OR, 0.68 [CI, 0.46 to 1.02]) but inconclusive for bleeding risk (OR, 0.82 [CI, 0.37 to 1.78]). For warfarin versus aspirin, moderate evidence favored warfarin (OR, 0.66 [CI, 0.45 to 0.99]), with inconclusive evidence for more major bleeding (OR, 1.61 [CI, 0.75 to 3.44]). The evidence suggested that adjusted-dose warfarin was more efficacious for stroke prevention than low-dose warfarin (OR, 0.52 [CI, 0.25 to 1.08]) or low-dose warfarin plus aspirin (OR, 0.44 [CI, 0.14 to 1.39]) but increased major bleeding (OR, 1.4 [CI, 0.72 to 2.7]).

Two trials of secondary prevention evaluated warfarin versus aspirin (11, 24). In 1 trial, the patients were stratified by their eligibility for warfarin therapy. It was found that among the warfarin-eligible patients, warfarin was more efficacious for stroke prevention (OR, 0.38 [CI, 0.22 to 0.66]; $P = 0.001$) but led to more episodes of major bleeding (OR, 4.1 [CI, 1.2 to 14]; $P = 0.029$) than did placebo. For the warfarin-ineligible patients, no difference in efficacy or bleeding risk was demonstrated when comparing aspirin with placebo.

For specific groups of patients, the absolute reduction in stroke rate with warfarin compared with aspirin was low in younger patients (mean age, 65 years) compared with older patients (5.5 per 1000 person-years vs. 15 per 1000 person-years, respectively). The evidence suggests that for persons with a low risk for stroke, aspirin may be useful. There is insufficient published evidence regarding the use of other antithrombotic agents. A single study of low-molecular-weight heparin versus placebo was inconclusive for stroke risk, and neither group had any major hemorrhagic events.

Recommendation 2: Patients with atrial fibrillation should receive chronic anticoagulation with adjusted-dose warfarin, unless they are at low risk of stroke or have a specific contraindication to the use of warfarin (thrombocytopenia, recent trauma or surgery, alcoholism). Grade: 1A

Clinical prediction rules have been developed on the basis of existing literature and have been validated for estimating risk for stroke in patients with atrial fibrillation (25). In one, a point system was developed and validated by using the following risk factors: recent congestive heart failure (that is, active within the past 100 days or documented by echocardiography), hypertension (systolic or diastolic), age of at least 75 years, diabetes mellitus, and history of stroke or transient ischemic attack. A scoring system called $CHADS_2$, an acronym for the above-mentioned risk factors, was developed. Each risk factor is assigned 1 point except for history of stroke or transient ischemic attack, which is assigned 2 points. The total number of points is 6 (**Table 2**). A score of 0 to 1 was designated as low risk; a score of 2 to 3 was designated as moderate risk; and a score of 4, 5, or 6 was designated as high risk.

Aspirin may be useful for patients with atrial fibrillation and a low risk for stroke, but the evidence is inconclusive. The evidence is unclear about the course to take when a patient spontaneously converts to sinus rhythm, but there is a suggestion that continued anticoagulation is appropriate. There is currently insufficient evidence to support the use of low-molecular-weight heparin or other antiplatelet agents in the management of atrial fibrillation.

SECTION 3: EFFICACY OF DIFFERENT AGENTS FOR RATE CONTROL

The AHRQ-funded evidence report found 48 trials assessing 17 different agents for rate control in atrial fibrillation (2). In the background paper, the authors concentrated on studies of digoxin, calcium-channel blockers, and β-blockers (2). The studies comparing digoxin with placebo were inconsistent, particularly during exercise (26–32). The nondihydropiridine calcium-channel blockers diltiazem and verapamil were more effective than placebo or digoxin in reducing the ventricular rate both at rest and during exercise (33–47). Studies evaluating β-blockers (39, 47–55) found improvement in both resting and exercise rate control for atenolol and metoprolol. Results with other

β-blockers were less consistent, and results evaluating exercise tolerance for all β-blockers were inconsistent.

Studies of combinations found that digoxin plus diltiazem, digoxin plus atenolol, and digoxin plus betaxolol were effective both at rest and with exercise. Labetalol, even in combination with digoxin, was ineffective at rest but effective with exercise.

Side effects were inconsistently reported in the trials, and most trials excluded patients with congestive heart failure. Most reports of side effects (dropout rates were poorly reported) came from the studies of calcium-channel blockers and digoxin.

Recommendation 3: For patients with atrial fibrillation, the following drugs are recommended for their demonstrated efficacy in rate control during exercise and while at rest: atenolol, metoprolol, diltiazem, and verapamil (drugs listed alphabetically by class). Digoxin is only effective for rate control at rest and therefore should only be used as a second-line agent for rate control in atrial fibrillation. Grade: 1B

Individual side effect profiles for all medications should be reviewed with patients and can provide guidance in the choice of agents for individual patients. Combinations of digoxin plus diltiazem, atenolol, or betaxolol have also been shown to be effective at rest and with exercise, but these may be better reserved for occasions when single-agent therapy has failed.

Section 4: Acute Conversion

Spontaneous Conversion to Sinus Rhythm and Reversion to Atrial Fibrillation after Cardioversion

While spontaneous conversion rates are not regularly reported in the trials, they can be determined from the conversion rates in the placebo groups. In the trials of pharmacologic conversion, the rates of spontaneous conversion in the placebo groups ranged from 0% to as high as 76%. Of the 21 trials that had placebo groups, 5 reported rates of spontaneous conversion of 0%, 10 reported rates between 1% and 33%, and 6 reported rates greater than 33%. In addition, the rates of reversion to atrial fibrillation can be extrapolated from the reported efficacy rates in the pharmacologic conversion trials. In many of these trials, fewer than 50% of patients were still in sinus rhythm at 3-month follow-up. These differences in rates of spontaneous conversion and reversion are most likely related to the characteristics of the patient samples. Some studies included patients with enlarged left atria, ischemic heart disease, hypertension, valvular disease, and differing durations of atrial fibrillation. Moreover, other patient characteristics, such as age, also play an important role. However, we are unable to quantify from these trials which patient characteristics would most reliably predict spontaneous conversion to sinus rhythm or reversion to atrial fibrillation.

Electrical Conversion

With the advent of external biphasic defibrillators, the immediate efficacy of direct-current external cardioversion exceeds 90%. The risk for thromboembolic events does not seem to differ between electrical and pharmacologic conversion. Patient preference needs to be taken into consideration when making the choice between electrical and pharmacologic conversion.

Antiarrhythmic Treatment before Electrical Cardioversion versus Electrical Conversion Alone

Of 8 randomized trials studying this question, 7 showed no increased efficacy with the use of quinidine, propafenone, or sotalol. One study showed increased efficacy with ibutilide, but ibutilide has a higher risk for inducing ventricular arrhythmia.

Pharmacologic Conversion

A meta-analysis of 54 randomized clinical trials was done for the background paper. In the 36 trials that had a control group, the authors found strong efficacy for acute conversion of atrial fibrillation with ibutilide, flecainide, dofetilide, propafenone, and amiodarone and moderate evidence for the efficacy of quinidine (2). Evidence for the efficacy of sotalol and disopyramide was insufficient. In a limited number of comparative studies, flecainide was superior to propafenone and procainamide, propafenone was superior to amiodarone, amiodarone was superior to quinidine, and quinidine was superior to sotalol.

An important side effect of antiarrhythmic therapy for conversion of atrial fibrillation is the risk for inducing torsades de points. This risk becomes even more important when choosing whether to initiate therapy in an inpatient or outpatient setting. However, only 30 of the 54 reviewed trials of pharmacologic conversion reported on the incidence of ventricular arrhythmias during the studies, thus limiting the usefulness of these data. Of those that did report such incidence, no ventricular arrhythmias were found in patients taking amiodarone and procainamide, and rates were 2% or less in patients taking flecainide, propafenone, and sotalol. Rates of up to 9% were reported for ibutilide, and rates of 12% were reported for quinidine and dofetilide. Two studies found that most arrhythmias occurred in the first 24 to 72 hours. Adverse outcomes from arrhythmias related to acute cardioversion, although uncommon, are more frequent with pharmacologic cardioversion than with direct-current cardioversion.

There is no reliable way to predict which patients are more at risk for arrhythmia, and this issue becomes even more important when deciding on the setting (inpatient or outpatient) for acute cardioversion. While it is common practice to stratify patients' risk according to the presence of structural heart disease, there is insufficient evidence to support this as a formal recommendation. Moreover, evidence of the relative safety of inpatient versus outpatient cardioversion is not available, so no recommendations can be made in this area.

Recommendation 4: For those patients who elect to undergo acute cardioversion to achieve sinus rhythm in atrial fibrillation, both direct-current cardioversion (Grade: 1C+)

and pharmacological conversion (Grade: 2A) *are appropriate options.*

While there are good data to support the use of both direct-current and pharmacologic conversion, there are no data on the efficacy of one method over the other because no head-to-head trials have compared them. It should be noted, however, that long-term effectiveness in maintaining sinus rhythm is moderate to low for both methods. For acute pharmacologic conversion of atrial fibrillation, strong evidence supports the efficacy of ibutilide, flecainide, dofetilide, propafenone, and amiodarone and moderate evidence supports the efficacy of quinidine. Antiarrhythmic therapy before electrical cardioversion does not improve the efficacy of acute conversion, although it may be used when maintenance therapy will be used after cardioversion. Adequate safety data are not available to make recommendations regarding the setting of cardioversion.

SECTION 5: THE ROLE OF ECHOCARDIOGRAPHY IN THE ACUTE CONVERSION OF ATRIAL FIBRILLATION

Transesophageal Echocardiography

Transesophageal echocardiography has been used before cardioversion as a means of stratifying patients for risk for thromboembolism. The Assessment of Cardioversion Using Transesophageal Echocardiography (ACUTE) study randomly assigned patients to a transesophageal echocardiography–guided strategy with short-term precardioversion and 4-week postcardioversion anticoagulation or to "conventional therapy" (3 weeks of precardioversion anticoagulation and 4 weeks of postcardioversion anticoagulation) (56). The primary end points of stroke, transient ischemic attack, or peripheral embolism did not differ between the groups. Statistically significantly more bleeding occurred in the conventional therapy group. Also, the transesophageal echocardiography group had a shorter time to cardioversion and a higher initial success rate. However, maintenance of sinus rhythm at 8 weeks was similar in both groups.

Measurement of Left Atrial Size

Transthoracic echocardiography has been used to predict the likelihood of successful conversion by measuring the left atrium. Only 6 trials of acute cardioversion reported on left atrial size. Of these, 5 found an inverse relationship between left atrial size and success of conversion. The data from the trials could not be combined, and therefore it is difficult to determine with any rigor whether there is a threshold of left atrial size above which cardioversion should not be attempted. The data can qualitatively support only the current clinical impression that the larger the atrium, the less likely cardioversion will be successful. There is also too little evidence to answer the question of whether left atrial size can help predict the likelihood of successful maintenance of sinus rhythm. Therefore, we conclude that, in patients who elect to undergo cardioversion, there is insufficient evidence to recommend the routine measurement of left atrial size to predict success. However, transthoracic echocardiography can still be useful in evaluating left ventricular function or hypertrophy.

Recommendation 5: Both transesophageal echocardiography with short-term prior anticoagulation followed by early acute cardioversion (in the absence of intracardiac thrombus) with postcardioversion anticoagulation versus delayed cardioversion with pre- and postanticoagulation are appropriate management strategies for those patients who elect to undergo cardioversion. Grade: 2A

In trials comparing the conventional approach of 3 weeks of anticoagulation before cardioversion followed by 4 weeks of anticoagulation after cardioversion and transesophageal echocardiography–guided early cardioversion with up to 3 weeks of anticoagulation after cardioversion, no differences in the end points of stroke, transient ischemic attack, or peripheral embolism have been seen. However, rates of minor and major bleeding events were higher with the conventional strategy. The choice between the 2 strategies should be based on patient preference and clinical situation, including contraindications to transesophageal echocardiography or availability of this technology.

SECTION 6: MAINTENANCE THERAPY

The background paper describes the results of a meta-analysis of 35 randomized trials of 8 antiarrhythmic agents used for maintenance of sinus rhythm in patients with atrial fibrillation (2). Twenty of these trials had a control arm. The results found strong evidence for the efficacy of amiodarone, disopyramide, propafenone, and sotalol and moderate evidence for the efficacy of flecainide, quinidine, and azimilide. Comparison trials found amiodarone to be more efficacious than propafenone and sotalol.

Adverse side effects are important to consider in choosing whether to use maintenance antiarrhythmic therapy and in choosing which medication to use. In particular, the risk for torsades de pointes and other ventricular arrhythmias should be considered. However, the true risks of each antiarrhythmic agent are not well elucidated in the literature. In the review of clinical trials for these guidelines, only 18 of the 35 studies of maintenance therapy reported the incidence of ventricular arrhythmias (2). No ventricular arrhythmias were reported with amiodarone or disopyramide. Although there also were no ventricular arrhythmias found in studies evaluating flecainide, most studies excluded patients with previous myocardial infarction because flecainide was contraindicated. Ventricular arrhythmias were found in 0% to 3% of patients treated with propafenone, 0% to 5% of those treated with sotalol, and 0% to 12% of those treated with quinidine. Other side effects prompted cessation or dose changes in 50% to 60% of patients treated with quinidine or disopyramide and 10% to 25% of patients treated with propafenone, flecainide, amiodarone, or sotalol. Of note, in the largest trial,

which involved 201 patients treated with amiodarone, this medication was discontinued because of suspected pulmonary toxicity in 4 patients, hypothyroidism in 2 patients, hyperthyroidism in 1 patient, and other reasons in 2 patients (57).

Recommendation 6: Most patients converted to sinus rhythm from atrial fibrillation should not be placed on rhythm maintenance therapy since the risks outweigh the benefits. In a selected group of patients whose quality of life is compromised by atrial fibrillation, the recommended pharmacologic agents for rhythm maintenance are amiodarone, disopyramide, propafenone, and sotalol (drugs listed in alphabetical order). The choice of agent predominantly depends on specific risk of side effects based on patient characteristics. Grade: 2A

All agents have some potential for both minor and serious side effects. This suggests the need for careful consideration of the relative risks and benefits of an aggressive approach to maintaining sinus rhythm versus the alternate strategy of rate control and stroke prevention before beginning therapy. Amiodarone has more noncardiac side effects than the other recommended agents but is considered safer in patients with congestive systolic heart failure and left ventricular hypertrophy. Sotalol and amiodarone are considered safest in patients with coronary artery disease (2). For carefully selected patients whose quality of life is substantially compromised by atrial fibrillation, the benefits of maintenance therapy may offset the risks.

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This manuscript was approved by the ACP Board of Regents on 31 March 2003 and by the AAFP Board of Directors on 29 April 2003.

Note: Clinical practice guidelines are "guides" only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment. All ACP clinical practice guidelines are considered automatically withdrawn, or invalid, 5 years after publication, or once an update has been issued.

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Grant Support: Financial support for the development of this guideline came exclusively from the AAFP and ACP operating budgets.

Potential Financial Conflicts of Interest: None disclosed.

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APPENDIX

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