Atrial Fibrillation and Atrial Flutter: Medical Management

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KEYWORDS

• Atrial fibrillation • Atrial flutter • Antiarrhythmic drugs • Elderly

KEY POINTS

- Atrial fibrillation and atrial flutter are common arrhythmias in the elderly.
- Rate control can be achieved with β-blockers, calcium channel blockers, and digoxin, and lenient rate control (resting heart rates of <110 bpm) seems to be an acceptable alternative to strict rate control.
- Antiarrhythmic agents are chosen based on the side effect profile, and dose adjustments are often required for age and renal function.
- Polypharmacy in the elderly is common, and drug interactions must be carefully taken into account when adjusting doses.
- Rate control and rhythm control strategies are associated with equivalent mortality and quality of life outcomes; therefore, in asymptomatic or minimally symptomatic patients, rate control is a reasonable therapeutic strategy.

INTRODUCTION

Atrial fibrillation (AF) and atrial flutter (AFL) are common cardiac rhythm disturbances that incur significant morbidity and mortality.[1,2] They are primarily disorders associated with aging. In a study of long-term care residents whose average age was 84 years, the prevalence of AF was 11% in women and 14% in men.[3] Currently, it is estimated that 3 million people in the United States have AF. This number is projected to double by the year 2050, with 50% of affected individuals older than the age of 80.[1] Age-related changes in the heart, including diastolic dysfunction and atrial remodeling, and increased incidence of hypertension and diabetes may account for the strength of association between age and AF. AF accounts for more cardiovascular hospitalizations than heart failure, atherosclerotic heart disease, or stroke.[4] In a retrospective study of Medicare patients 65 years and older, more than half of the patients diagnosed with AF were hospitalized within the first year of diagnosis, with a readmission rate of 43.7% over a mean of 24 months.[5]

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The management of AF and AFL is multifaceted. Prevention of thromboembolism and stroke, control of heart rate, and the restoration of sinus rhythm are three major areas of therapy that should be addressed for each patient. Numerous methods are available to achieve each goal, and each method has a risk-benefit ratio that must be considered on an individual basis. Comorbidities, potential for drug intolerance, drug interactions caused by polypharmacy, and higher risk for procedural complications are among the factors that make management of AF and AFL challenging in older patients (**Box 1**). Prevention of thromboembolism and invasive methods of therapy are addressed elsewhere in this issue. This article reviews the most recent data on the medical management of AF and AFL in the elderly, including an in-depth evaluation of pharmacologic agents available for rate and rhythm management of AF and AFL, and a discussion of rate versus rhythm control.

RELATIONSHIP BETWEEN AF AND AFL

The pathophysiologic relationship between AF and AFL is not completely clear. AF is generally recognized as a result of chaotic atrial rhythm involving multiple microreentrant circuits within the atria, whereas AFL is a more organized, macroreentrant rhythm. The most common type of AFL has negative flutter waves ("saw-tooth pattern") in the inferior leads on the 12-lead electrocardiogram (ECG), and involves a reentrant circuit with a critical area of slow conduction in the isthmus bordered by the tricuspid valve, inferior vena cava, and coronary sinus (isthmus-dependent AFL).

AF was first observed to spontaneously organize into AFL in 1924.[6] It has also been noted that some antiarrhythmic drugs can convert AF to AFL.[7] Isthmus-dependent AFL is amenable to radiofrequency ablation, with long-term success rates approaching 80%.[8] For patients in whom AF is observed to convert to AFL with antiarrhythmic drugs, a hybrid approach, with ablation of AFL and continuation of antiarrhythmic drugs, has been advocated to control AF. Unfortunately, long-term follow-up demonstrates AF recurrences in 90% of patients.[9] In one study of patients with no documented AF before AFL ablation, the incidence of AF was 50% at a mean follow-up of 30 months.[10]

Box 1
Information required for drug choice and dosing in the elderly

- Age
- Gender
- Body weight
- Body mass index
- Creatinine clearance
- Hepatic function
- Ejection fraction
- Heart failure functional status
- Comedications, including prescription, over-the-counter, and herbal preparations
- Intake of grapefruit or grapefruit juice
- Baseline electrocardiogram measurements of QRS and QT interval

Because of the close relationship between AF and AFL, although they are distinctly different arrhythmias, similar management strategies are applied to both. In general, the two main approaches to medical management of AF and AFL are rate control (ie, controlling the ventricular response rate) and rhythm control (ie, attempting to maintain sinus rhythm). As discussed elsewhere in this issue, most older adults require long-term anticoagulation, regardless of the choice of rate or rhythm control.

RATE CONTROL

Effective control of ventricular rate during AF and AFL is a primary goal in acute and chronic phases of management. Rate control is crucial for the relief of symptoms and the prevention of tachycardia-mediated cardiomyopathy. Guidelines suggest targeting a resting heart rate of 60 to 80 beats per minute, and a peak rate with exercise of 90 to 115 beats per minute.[1]

β-Blockers

β-Blockers are highly effective in controlling ventricular rates in AF in the acute and chronic settings. β-Blockers are not effective in the conversion of AF to sinus rhythm. The onset of action with intravenous β-blockers for rate control is usually within minutes. Because of their antisympathetic actions, oral β-blockers are the most effective drugs in controlling ventricular rates during exertion. β-Blockers also have the advantage of reducing mortality in patients with coronary artery disease.[11] β-Blockers given before cardiac surgery have been shown to decrease the incidence of postoperative AF.[12] For acute rate control, metoprolol and atenolol may be given as intravenous boluses, and esmolol may be administered as a continuous infusion. In addition to metoprolol and atenolol, propranolol, timolol, nadolol, bisoprolol, nebivolol, and carvedilol are available in the United States and may be used to maintain effective heart rate control. β-Blockers are contraindicated in patients with significant bradycardia (heart rate <40–45 bpm), atrioventricular (AV) nodal block, hypotension, bronchospasm, or decompensated heart failure. Additional side effects may include decreased exercise tolerance, fatigue, low mood, sleep disturbances, and sexual dysfunction.

Elderly patients with sinoatrial dysfunction are particularly prone to development of bradyarrhythmias when receiving β-blockers. Compared with younger men, a greater reduction in exercise heart rate at a given atenolol concentration has been reported in elderly men. Decreased number of β-adrenoreceptors and blunted β-adrenoreceptor responsiveness have been implicated as possible mechanisms.[13] A genetic polymorphism of the β_1-adrenergic receptor ADRB1 has been associated with favorable response to all rate-controlling agents. The presence of the polymorphism is postulated to have synergic effects to calcium channel blockers and digoxin. Carriers of the genetic variant seem to require lower doses of medication for rate control compared with noncarriers.[14]

Calcium Channel Blockers

Like β-blockers, the nonhydropyridine calcium channel blockers verapamil and diltiazem act directly on the AV node to slow conduction. They are not effective in converting AF to sinus rhythm. Intravenous verapamil and diltiazem have a rapid onset of action and are effective in acutely controlling the ventricular rate. Verapamil is more negatively inotropic than diltiazem, and it is also more likely to cause hypotension. Long-term use of these agents should be avoided in patients with decreased left ventricular systolic function. Diltiazem, 0.25 mg/kg, may be given intravenously every

5 to 10 minutes for acute rate control. If needed, this may be followed by a continuous infusion of 5 to 15 mg/h, titrated to achieve the desired heart rate. Verapamil may be given intravenously in 2.5- to 5-mg boluses. Oral maintenance doses for diltiazem and verapamil range from 120 to 360 mg daily in divided doses or as long-acting formulations. Major side effects include hypotension, bradycardia, heart block, and heart failure exacerbations. Constipation is a common side effect in older adults, especially with verapamil. Lower-extremity edema is also common, and may be erroneously attributed to worsening heart failure.

Digoxin

Neither intravenous nor oral digoxin facilitates conversion to sinus rhythm.[15] Digoxin is used primarily to control the ventricular response rate. However, because effective rate control with intravenous digoxin may take 12 hours or longer,[16] there is little role for intravenous digoxin in the acute setting. Digoxin slows ventricular rate by enhancing vagal tone, and the effect is easily overcome by sympathetic activity. Therefore, digoxin is generally not effective in the postoperative setting or in very active patients.

As monotherapy, digoxin is potentially useful in elderly and sedentary patients in whom hypotension, severe heart failure, or other conditions preclude the use of β-blockers or calcium channel blockers. Digoxin is most effective when used in combination with other drugs. In a clinical trial comparing digoxin, diltiazem, atenolol, and the combination of diltiazem or atenolol with digoxin, digoxin plus atenolol, 50 mg daily, provided the most effective rate control.[17]

The usual maintenance dose of digoxin is 0.125 to 0.375 mg per day. Decreased volume of distribution and glomerular filtration predispose elderly patients to an increased risk for digoxin toxicity, which may manifest as heart block, bradycardia, or ventricular arrhythmias. In elderly patients with reduced creatinine clearance (CrCl), it is generally recommended that a daily dose of 0.125 mg per day is sufficient. Because the cardiac effects of digoxin are potentiated by hypokalemia, hypomagnesia, and hypercalcemia, serum levels of these electrolytes should be maintained within the normal range. In addition, many medications increase the plasma concentration of digoxin, so careful scrutiny for potential drug interactions is extremely important to avoid toxicity (**Table 1**).

RHYTHM CONTROL

Restoration and maintenance of sinus rhythm is frequently necessary for symptomatic relief. Conversion of AF and AFL to sinus rhythm is best achieved with electrical cardioversion, and maintenance of sinus rhythm typically requires the use of antiarrhythmic drugs. Rhythm control becomes more difficult with prolonged duration in AF, depressed systolic function, severe diastolic dysfunction, and larger atrial size.

In patients with AF and rapid ventricular rate who are hemodynamically unstable, immediate electrical cardioversion is indicated. In stable patients, electrical cardioversion may be electively performed with low risk of thromboembolic events if the duration of AF is less than 48 hours, or if patients are on warfarin with therapeutic INRs for at least 3 consecutive weeks. If the duration is unknown, if patients are not on long-term anticoagulation, or if subtherapeutic INRs have recently been documented, a transesophageal echocardiogram is recommended to rule out the presence of left atrial thrombus before cardioversion. Anticoagulation with warfarin must be continued for a minimum of 1 month after cardioversion because of continuing risk of thrombus formation from atrial stunning after cardioversion. In patients with risk factors for

Table 1
Potential major drug interactions

Drug	Plasma Concentration Increased By	Plasma Concentration Decreased By
Digoxin	Amiodarone Quinidine Propafenone Diltiazem Verapamil Erythromycin Itraconazole Dronedarone	
Metoprolol	CYP2D6 inhibitors: Quinidine Propafenone Amiodarone Paroxetine Dronedarone	
Dofetilide	Inhibition of renal tubular secretion: Hydrochlorothiazide Cimetidine Ketoconazole Trmethoprim Increased hepatic blood flow (increased absorption): Verapamil	CYP3A4 inducers: Carbamazepine Phenytoin Rifampin St John's Wort
Disopyramide Diltiazem Dronedarone	Cyp3A4 inhibitors: Itraconazole Ketoconazole Clarithromycin Grape fruit juice	CYP3A4 inducers: Carbamazepine Phenytoin Rifampin St John's Wort

stroke, warfarin should be continued indefinitely.[18] Elective cardioversion with the new anticoagulants, rivaroxiban and dabigatran, has not been well studied. However, continuous use of dabigatran for a minimum of 3 weeks before cardioversion does not seem to be associated with increased risk of stroke compared with warfarin.[19] Electrical conversion of AFL usually requires lower energy than AF. Occasionally, AFL can be terminated through rapid atrial pacing, which may be delivered by the atrial lead in patients with dual-chamber pacemakers or defibrillators.

Some antiarrhythmic agents may convert AF or AFL to sinus rhythm. Regardless of the method of conversion, whether electrical, pacing, or pharmacologic, appropriate anticoagulation status must be ascertained before initiation of therapy.

ANTIARRHYTHMIC DRUGS

Challenges in the Elderly

Administration of oral antiarrhythmic agents in elderly patients is frequently complicated by comorbidity, diminished drug clearance, compliance issues, and polypharmacy leading to drug interactions. Aging is usually associated with increases in total body fat and decreases in lean body mass and total body water. These changes can affect the volume of distribution of lipophilic and hydrophilic drugs, and may necessitate a reduction in dosages. Therapeutic drug monitoring of antiarrhythmic drugs has some role in the treatment of elderly patients. Measuring the plasma

concentrations of these drugs may help to clarify whether dosage adjustments are possible when pharmacotherapy fails. However, monitoring plasma concentrations does not minimize the necessity of ECG monitoring for evaluation of QRS and QT intervals. Furthermore, significant signs of clinical toxicity can occur even at plasma levels that are at the lower end of the accepted therapeutic range.[20]

Vaughn-Williams Classification

The Vaughn-Williams Classification was introduced in 1970 and is one of the most widely used classification schemes for antiarrhythmic agents. This scheme classifies a drug based on the primary mechanism of its antiarrhythmic effect. It should be noted, however, that many antiarrhythmic drugs have multiple mechanisms of action. Class II (β-blockers) and intravenous (calcium channel blockers) are used for rate control and have been discussed previously. Class I and III drugs are used for rhythm control, and are discussed next.

Vaughn-Williams Class IA

Class IA antiarrhythmic drugs (quinidine, procainamide, and disopyramide) are sodium and potassium channel blockers that increase action potential duration and QT interval. They are not as commonly used nowadays as they were in the past, because they are only moderately effective and are associated with significant side effects. Because they can prolong the QT interval, the most serious side effect from these agents is torsades de pointes ventricular tachycardia (VT). Quinidine may be given as quinidine sulfate at 200 to 400 mg every 6 hours or as quinidine gluconate at 324 to 648 mg every 8 to 12 hours. It is frequently associated with nausea or diarrhea, and it has also been associated with increased mortality, presumably because of proarrhythmia.[21] The efficacy of intravenous procainamide for chemical conversion of recent-onset AF to sinus rhythm is unproved.[22] Procainamide is given orally at 1 to 6 grams per day in divided doses. Prolonged use of procainamide may be associated with a systemic lupus-like syndrome. Disopyramide, given 100 to 300 mg every 6 to 8 hours, has anticholinergic effects that may be useful for AF that is triggered by increased vagal tone. However, the anticholinergic actions may exacerbate glaucoma or urinary dysfunction in the elderly. Disopyramide also has potent negative inotropic action that precludes its use in patients with severe left ventricular dysfunction and chronic heart failure.

Vaughn-Williams Class IB

Class IB agents, such as mexiletine and lidocaine, have no effect on atrial tissues and are not used for treatment of AF or AFL.

Vaughn-Williams Class IC

Class IC drugs (flecainide and propafenone) are predominantly sodium channel blockers. They prolong the action potential duration to a significantly greater extent than they prolong the QT interval. As a result, cardiac toxicity manifests predominantly as widened QRS intervals. This effect is more pronounced at faster heart rates, and is more prominent with flecainide than with propafenone. Once maintenance dose has been achieved, an exercise stress test is recommended to monitor for QRS widening at higher heart rates. Flecainide and propafenone may convert AF to AFL. The slower flutter waves may then be conducted through the AV node with a 1:1 relationship, resulting in a rapid ventricular rate. Therefore, it is important to use AV nodal blocking agents concomitantly with class IC drugs. Propafenone also has β-blocking properties, and may exacerbate bradycardia.

Although these agents are effective in maintaining sinus rhythm, their safety profile has been in question since the publication of the Cardiac Arrhythmia Suppression Trial.[23] This study showed increased mortality in patients who were prophylactically treated with flecainide or encainide for suppression of premature ventricular complexes after uncomplicated myocardial infarctions. Whether flecainide or propafenone increases mortality in patients treated for atrial arrhythmias is unknown. However, the results of the Cardiac Arrhythmia Suppression Trial study have been generalized to patients with coronary artery disease or any structural heart disease, and class IC agents are not recommended in these populations (including most elderly patients). In patients with normal hearts, however, these drugs offer few side effects and have an excellent safety profile. The main side effects are sinus node depression and bradycardia.

Flecainide is given at 50 to 200 mg orally twice a day; many elderly patients only require 50 mg twice a day. The starting dose of propafenone is 150 mg every 8 to 12 hours. Metabolism of flecainide and propafenone are dependent on the activity of the CYP2D6 isoenzyme. Approximately 5% to 10% of the white population has mutations of this isoenzyme, making them "poor metabolizers" of the drugs, requiring a reduction in dose.[24]

Vaughn-Williams Class III

Class III drugs (sotalol, dofetilide, and ibutilide) are predominantly potassium channel blockers, with a tendency to cause QT prolongation. Torsade de pointes VT is a significant potential side effect from these agents. Sotalol is a racemic mixture with β-blocking (l-sotalol) and class III antiarrhythmic (d-sotalol) properties. Oral dosing is usually 80 to 160 mg twice a day. D-sotalol alone has been shown to increase mortality in postinfarction patients,[25] and is not clinically available. Sotalol is renally excreted, and the risk of QT prolongation and torsade de pointes VT is higher in patients with decreased CrCl. These issues are of particular importance in elderly women, in whom longer QT intervals may be noted at baseline. Sotalol is contraindicated in patients with CrCl less than 40 mL/min and should be administered once daily in patients with CrCl of 40 to 60 mL/min. Initiation of sotalol, especially in elderly patients, should ideally be in the hospital setting for monitoring of QT intervals and creatinine. Sotalol may exacerbate chronic heart failure, and it is not recommended in patients with acute heart failure exacerbations.

The main advantages of dofetilide over sotalol are its safety profile in patients with severe left ventricular dysfunction or chronic heart failure and lower likelihood to cause significant bradycardia.[26,27] Initiation of dofetilide requires hospitalization with continuous telemetry monitoring for a minimum of six doses. Dofetilide dosing does not need to be adjusted for age, but is dependent on the baseline QT interval and CrCl. A baseline corrected QT (QTc) interval of more than 440 milliseconds, or more than 500 milliseconds with a bundle branch block or paced rhythm, precludes the use of dofetilide, as does a CrCl of less than 20 mL/min. Initial dose of dofetilide is 500 μg twice a day if the CrCl is more than 60 mL/min, 250 μg twice a day if the CrCl is 40 to 60 mL/min, and 125 μg twice a day if the CrCl is 20 to 40 mL/min. A 12-lead ECG must be obtained 1 to 2 hours after each dose and the QT interval carefully measured. If the QTc is more than 500 milliseconds after one dose, the subsequent dose must be reduced by half. If the subsequent ECG shows QTc more than 500 milliseconds, then the drug must be discontinued.[28]

Ibutilide is currently the only intravenous drug approved for chemical conversion of AF. It is more effective when used in AF of short duration (<7 days), and more effective in AFL than AF.[22] Ibutilide is associated with QT prolongation and a 4% to 8% risk of

torsade de pointes VT, especially in the first 2 to 4 hours after administration of the drug. The risk for VT is higher in patients with cardiomyopathy and chronic heart failure. Ibutilide is given as intravenous bolus at a dose of 1 mg over 10 minutes or until conversion, whichever occurs first. It should only be given under carefully monitoring by personnel familiar with the drug, and an external defibrillator should be readily available in case of torsades de pointes VT. Patients must be monitored on telemetry for at least 4 hours after being given the drug. Ibutilide is not available in oral form for maintenance of sinus rhythm.

Amiodarone

Amiodarone is a complex drug that blocks sodium, potassium, calcium, and β-receptors. Intravenous amiodarone may facilitate conversion to sinus rhythm, although usually only after 48 hours of treatment.[29] Oral amiodarone can also convert a small proportion of patients with AF to sinus rhythm.[30] Prophylactic amiodarone given for a minimum of 7 days before cardiac surgery has been shown to reduce postoperative AF, thereby shortening hospital stay and reducing hospitalization costs.[31] Amiodarone may be used safely in patients with a history of myocardial infarction or left ventricular dysfunction. A loading dose of amiodarone is usually required to achieve steady-state blood levels. For oral therapy, the usual starting dose is 400 mg three times a day, with subsequent dosage reductions over a period of several weeks to a maintenance dose of 200 mg per day. Maintenance doses as low as 50 to 100 mg per day may be sufficient in the elderly. Amiodarone is a highly lipophilic drug for which fat is a major site of distribution.[32] In elderly patients with high body fat, a larger loading dose may be required.

Short-term use of amiodarone is usually well tolerated, but side effects are common during long-term administration. Major side effects include thyroid dysfunction, liver function abnormalities, pulmonary toxicity, photosensitivity, skin discoloration, bradycardia, and neurologic dysfunction, all of which are usually reversible with early detection and discontinuation of the drug. Before initiation of amiodarone, baseline thyroid function tests, liver function tests, chest radiograph, and pulmonary function tests should be obtained. Laboratory tests should be followed every 6 months. Chest films and pulmonary function tests are usually followed every 1 to 2 years, or whenever patients develop symptoms of shortness of breath. Amiodarone-induced bradycardia is more common in older patients, especially those with prior myocardial infarctions or sinus node dysfunction, and may require pacemaker implantation.[33] Although prolongation of the QT interval may occur, torsades de pointes VT is less common with amiodarone than with other antiarrhythmic drugs. Amiodarone is excreted through the skin, and has an elimination half-life of 1 to 2 months. In elderly patients with higher total body fat, clearance from the circulation may take even longer.

Dronedarone

Dronedarone is a relatively new antiarrhythmic drug that is pharmacologically related to amiodarone but lacks the iodine moiety that is associated with thyroid and pulmonary side effects.[34] Dronedarone is given at a set dose of 400 mg twice a day. Initial studies in patients with a mean age of 63 years and paroxysmal AF showed that dronedarone was better at maintaining sinus rhythm and ventricular rate control than placebo.[35] In direct comparison with amiodarone, dronedarone was associated with more AF recurrence, although amiodarone was associated with more side effects and higher rate of drug discontinuation.[36] Dronedarone has been shown to reduce the incidence of hospitalization for cardiovascular causes and death compared with placebo.[37] The reduction in cardiovascular events led to the

hypothesis that the benefits of dronedarone may extend beyond rhythm control. This hypothesis was tested in the PALLAS trial, which showed that administration of dronedarone in patients with permanent AF was in fact associated with an increase in the rates of heart failure hospitalization, stroke, and death.[38] This trial is particularly relevant to elderly patients because patients 75 years or older constituted more than 50% of the study population. Elderly patients with asymptomatic permanent AF should not be treated with dronedarone for rate control. Dronedarone is also contraindicated in patients with severe left ventricular systolic dysfunction or recent heart failure exacerbation, because it has been shown to increase total mortality in such patients.[39]

Choice of Antiarrhythmic Drugs

The first step in choosing an antiarrhythmic agent for a patient with AF is to determine the presence or absence of structural heart disease. In patients without structural heart, flecainide or propafenone, along with an AV nodal blocking agent, are an excellent first choice. Disopyramide may be used in patients without known glaucoma or urinary retention if AF is triggered by high vagal tone. In patients with structural heart disease, including significant left ventricular hypertrophy, in conjunction with normal baseline QT interval and renal function, sotalol is an appropriate first-choice agent. In patients with active heart failure or baseline bradycardia, dofetilide is a reasonable alternative. In elderly patients, presence of heart disease and decreased renal function frequently preclude the use of many of the previously mentioned agents. As a result, amiodarone is commonly used in older patients. Dronedarone is a reasonable alternative to amiodarone in patients with paroxysmal AF in the absence of heart failure, although its efficacy seems to be inferior to amiodarone.

RATE VERSUS RHYTHM CONTROL

Elderly patients were not well represented in major trials evaluating the comparative effectiveness of rate versus rhythm control strategies. The mean age of patients in these trials was less than 70 years. The largest trial, AFFIRM, was an international study that randomized asymptomatic patients to rate versus rhythm control.[40] There was no difference in the primary outcome of overall mortality between these two groups. The PIAF trial[41] studied symptomatic patients with persistent AF. During follow-up, quality of life improved for rate and rhythm control groups, but there was no difference between groups. The AF-CHF trial studied the effects of rate or rhythm control in patients with left ventricular ejection fractions of 35% or less, and found that even in this high-risk population, there was no difference between groups in the primary endpoint of time to death from cardiovascular causes.[42] The results of other major studies are shown in **Table 2**, with no significant differences in major composite endpoints of death, thromboembolic events, or major bleeding between rate and rhythm control. The RACE II trial importantly showed that patients treated with “lenient” rate control, defined as a resting heart rate of less than 110 bpm, have the same quality of life scores as patients treated with “strict” rate control, defined as a resting heart rate of less than 80 bpm and exercise heart rates of less than 110 bpm.[43] The results of these trials suggest that for most patients with minimal symptoms, rate control is an acceptable therapeutic option, and does not increase mortality or major cardiovascular events. Additionally, lenient rate control is a very reasonable therapeutic approach in elderly patients.

Table 2
Major studies of rate versus rhythm control

Study	# Rhythm Control	# Rate Control	Mean Age (y)	% Women	Mean Follow-up	% SR in Rhythm Control Group at Follow-up	Primary Endpoint	Result
AFFIRM[40] (2002)	2033	2027	69	40	3.5 y	73	Overall mortality	No difference
RACE[44] (2002)	266	256	68	37	2.3 ± 0.6 y	39	Composite[a]	No difference
PIAF[41] (2003)	127	127	61	28	1 y	56	Quality of life	No difference
STAF[45] (2003)	100	100	65	40	19.6 ± 8.9 mo	23	Composite[a]	No difference
HOT CAFE[46] (2004)	104	101	60	35	1.7 ± 0.4 y	63.5	Composite[a]	No difference
AF CHF[42] (2008)	682	694	66	20	37 ± 19 mo	73	Time to death from CV causes	No difference

Abbreviations: AF CHF, Atrial Fibrillation and Congestive Heart Failure; AFFIRM, Atrial Fibrillation Follow-Up Investigation of Rhythm Management; CV, cardiovascular; HOT CAFÉ, How To Treat Chronic Atrial Fibrillation; PIAF, Pharmacologic Intervention in Atrial Fibrillation; RACE, Rate Control versus Electrical Cardioversion; SR, sinus rhythm; STAF, Strategies of Treatment of Atrial Fibrillation.

[a] Composite endpoints = death, thromboembolic events, major bleeding.

SUMMARY

AF and AFL are common arrhythmias in elderly patients. Medical management of AF in the elderly is particularly challenging, and every decision regarding the management of AF has an associated risk. An understanding of potential drug interactions, vigilance in assessing comorbidities, and knowledge of drug side effects are important factors in determining appropriate drugs and dosages for each individual patient.

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