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ONE MINUTE CONSULT
BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: Atrial fibrillation: Rate control or rhythm control?

A: Atrial fibrillation can be managed by either a rate control or a rhythm control strategy. Data as to which provides better clinical outcomes have been mixed.

Until now, rate control has been preferred, in view of the side effects of antiarrhythmic drugs and the noninferiority of rate control that was demonstrated in multiple studies.[1–4] However, rate control as the primary approach is now in question, and the pendulum is swinging in favor of rhythm control.

For patients with atrial fibrillation, the 3 principal goals of therapy are to control symptoms, prevent thromboembolism and stroke, and prevent tachycardia-mediated cardiomyopathy.[5] Maintaining sinus rhythm has many benefits, as it is more physiologic and maintains atrioventricular synchronicity with improved ventricular filling through "atrial kick," thereby improving exercise tolerance, relieving symptoms better, and preventing structural and electrical remodeling.[6] Therefore, even if direct evidence from randomized clinical trials is lacking in many types of patients, given the unpredictable long-term adverse effects of atrial fibrillation, rhythm control is generally the goal. Another factor pushing us in that direction is modern technology such as pulsed-field ablation, which has shown benefits and safety in preclinical and clinical studies.[7]

EVIDENCE FAVORING RATE CONTROL

Several landmark trials formed the basis of current guidelines for treating atrial fibrillation.[8]

The AFFIRM trial (Atrial Fibrillation Follow-up Investigation of Rhythm Management),[1] published in 2002, was one of the first large randomized controlled trials to compare rate control and rhythm control. It found no difference in survival outcomes between the strategies, and rates of hospitalization and adverse drug effects were significantly lower with rate control. In both study groups, most strokes occurred after warfarin was stopped or when the international normalized ratio was subtherapeutic. The mean age of the patients was 70, and therefore these results may not be applicable to younger patients.

Up to now, rate control has been preferred, but the pendulum is swinging in favor of rhythm control

The STAF study (Strategies of Treatment of Atrial Fibrillation)[2] yielded results similar to those of the AFFIRM trial in terms of both survival and hospitalizations.

The PIAF trial (Pharmacological Intervention in Atrial Fibrillation)[3] showed no significant difference in symptom improvement between the treatment groups, but the rhythm control group had more hospital admissions.

The RACE study (Rate Control vs Electrical Cardioversion for Persistent Atrial Fibrillation)[4] found more cardiovascular deaths and hospitalizations for congestive heart failure with rate control, while thromboembolic events, drug side effects, and pacemaker implantation were more frequent in the rhythm control group.

Of note, most of these trials were designed to evaluate the *noninferiority* of rate control compared with rhythm control, not *superiority*. Another consideration is that these trials were conducted almost 20 years ago, and rhythm control strategies—in particular, ablation—have since evolved.

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TABLE 1
Treatments for atrial fibrillation

Treatment	Indications	Contraindications
Rate control	Asymptomatic atrial fibrillation and rhythm control not favored (elderly patient, long-standing atrial fibrillation, markedly enlarged left atrium)	Avoid calcium channel blockers in patients with heart failure
Electric cardioversion	Symptomatic atrial fibrillation New-onset atrial fibrillation Low risk of thromboembolism: (< 48 hours since onset of atrial fibrillation, or at least 3 weeks of anticoagulation, or transesophageal echocardiography to rule out thrombus)	No anticoagulation or inability to obtain transesophageal echocardiography
Antiarrhythmic medications	Younger patient High cardiovascular risk Heart failure Failure of rate control therapy	Avoid propafenone and flecainide in those with structural heart disease and coronary heart disease Avoid dronedarone in persistent atrial fibrillation and congestive heart failure Avoid sotalol and dofetilide in renal failure
Catheter ablation	Younger patients Symptomatic atrial fibrillation, refractory to medical therapy Can be considered in heart failure	Marked left atrial dilation
Atrioventricular junction ablation and cardiac resynchronization therapy	Contraindication to ablation or failure of ablation Permanent atrial fibrillation Systolic heart failure with ejection fraction < 30%	Frail patient Expected survival < 1 year

EVIDENCE FAVORING RHYTHM CONTROL

Rhythm control strategies include antiarrhythmic drug therapy and catheter ablation.

The EAST-AFNET 4 (Early Treatment of Atrial Fibrillation for Stroke Prevention Trial)[9] reported that in patients with a diagnosis of atrial fibrillation within the past year and concomitant high-cardiovascular-risk conditions, treatment with drugs or catheter ablation was associated with lower risks of death from cardiovascular causes, stroke, or hospitalization for heart failure or acute coronary syndrome than usual care. Furthermore, there was no significant difference in length of hospital stay between the groups. The favorable results for rhythm control were likely due to including catheter ablation along with antiarrhythmic drugs as a rhythm control treatment.

The Get With The Guidelines—Heart Failure registry[10] study found that rhythm control was associated with lower risk of death at 1 year in patients age 65 and older with atrial fibrillation and heart failure with preserved ejection fraction.

Shojaee et al[11] found that, in patients who presented to the emergency department in rapid atrial fibrillation, amiodarone was superior to digoxin with regard to treatment success and quicker onset of action.

Delle Karth et al[12] compared amiodarone vs diltiazem in critically ill patients and found equivalent outcomes with either drug. However, more patients had to discontinue diltiazem therapy due to hypotension.

EVIDENCE ON CATHETER ABLATION VS MEDICAL THERAPY

Numerous randomized controlled trials have compared catheter ablation and medical therapy for

rhythm control in atrial fibrillation.

The CASTLE-AF (Catheter Ablation for Atrial Fibrillation With Heart Failure)[13] and **AATAC** (Ablation vs Amiodarone for Treatment of Persistent Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted Device)[14] trials included patients with atrial fibrillation and left ventricular systolic dysfunction. They showed that catheter ablation was associated with significantly lower rates of death from any cause or of hospitalization for worsening heart failure compared with medical therapy. CASTLE-AF compared catheter ablation vs medical therapy for rate or rhythm control, whereas AATAC compared catheter ablation vs amiodarone.

The CABANA trial (Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation)[15] included patients with and without left ventricular systolic dysfunction and an overall healthier cohort than in CASTLE-AF and AATAC. Catheter ablation did not show a significant reduction in death, disabling stroke, serious bleeding, or cardiac arrest compared with medical therapy at 12 months. These results were thought to be affected by lower-than-expected event rates and high crossover rates in the study. Per-protocol analyses, as opposed to intention-to-treat analyses, showed significant benefit with catheter ablation vs drug therapy with regard to both the primary and secondary end points. On subgroup analysis, the maximal benefit of catheter ablation was in younger patients.[16]

D'Angelo et al[17] performed a retrospective study and found results comparable to those of CABANA, with early referral for catheter ablation showing better outcomes as opposed to late referral.

The STOP-AF First[18] and **EARLY-AF** (Early Aggressive Invasive Intervention for Atrial Fibrillation)[19] trials found lower rates of recurrence of arrhythmia with cryoablation than with antiarrhythmic drug therapy.

Asad et al[20] performed a meta-analysis of the above-mentioned studies and several others comparing catheter ablation vs medical therapy for atrial fibrillation. The rate of all-cause mortality was lower with catheter ablation, a difference that was primarily driven by patients with atrial fibrillation and heart failure with reduced ejection fraction from the CASTLE-AF trial. Moreover, there were significant reductions in cardiovascular hospitalizations and recurrence of atrial arrhythmia with catheter ablation in patients both with and without heart failure.

INDIVIDUALIZED THERAPY

The choice of therapy should be individualized, as summarized in **(Table 1)**.

Rate control with a beta-blocker or calcium channel blocker may be preferred in patients with asymptomatic atrial fibrillation (whether paroxysmal, persistent, or permanent) and in patients in whom rhythm control may not be a good option, such as elderly patients, patients with long-standing atrial fibrillation, and those with markedly enlarged left atria. Calcium channel blockers are best avoided in patients with heart failure.

Since its invention, ablation has demonstrated the best outcomes with regard to mortality and morbidity

Rhythm control

Rhythm control may be preferable in patients who are younger, are at high cardiovascular risk, or have heart failure, or in patients for whom rate-control therapy has failed.

Cardioversion can restore sinus rhythm and can be repeated multiple times if unsuccessful at first. It can be used for patients with symptoms or with newly diagnosed atrial fibrillation. To lessen the risk of thromboembolism, patients must have had atrial fibrillation for less than 48 hours, must have been on anticoagulation for at least 3 weeks, or must undergo transesophageal echocardiography to rule out thrombus before cardioversion.[21]

Antiarrhythmic drug therapy. Occasionally, certain antiarrhythmic drugs may need to be started in the hospital to ensure patient safety, as they can lead to life-threatening arrhythmias. Amiodarone and dronedarone have the least-cardiotoxic adverse effects compared with other antiarrhythmic drugs. However, amiodarone has significant systemic effects, including liver, lung, and thyroid toxicity. Dronedarone has a better systemic adverse-effect profile than amiodarone, but it is associated with hepatotoxicity.

Dronedarone cannot be used in patients with heart failure, as a higher mortality rate has been reported in this subgroup when given dronedarone.[22] Moreover, the PALLAS study (Permanent Atrial Fibrillation Outcome Study Using Dronedarone on Top of Standard Therapy)[23] found that dronedarone was associated with higher rates of stroke, cardiovascular death, and readmission when used to treat permanent atrial fibrillation.

Amiodarone is the most commonly prescribed antiarrhythmic drug for atrial fibrillation, and when compared with other antiarrhythmics, including sotalol, dronedarone, propafenone, and flecainide, it was the most effective in maintaining sinus rhythm.[24–27]

Amiodarone, sotalol, and dofetilide can be safely used in patients with structural heart disease, but caution is advised for other antiarrhythmic drugs.

Propafenone and flecainide are good options in patients without structural heart disease.[28]

Catheter ablation. Since its invention, ablation has demonstrated the best outcomes with regard to mortality and morbidity. Trials that compared catheter ablation and drug therapy (for rate control or rhythm control) have consistently shown better outcomes with catheter ablation. It is a good option for patients who are younger, do not have left atrial dilation, have symptomatic atrial fibrillation, or have atrial fibrillation that is refractory to medical therapy.[29,30] It can be considered for patients who have heart failure and for those who have no symptoms, after shared decision-making.[31]

Ablate and pace. In cases in which atrial fibrillation persists despite multiple ablations or regular ablation is contraindicated, a possible next step is atrioventricular junction ablation with cardiac resynchronization therapy—ie, destroying the electrical link between the left atrium and left ventricle and putting in a pacemaker. Patients who underwent this "ablate-and-pace" procedure had a lower mortality rate than those who received control therapy in the APAF-CRT (Ablate and Pace for Atrial Fibrillation—Cardiac Resynchronization Therapy) trial.[32]

DISCLOSURES

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