A 61-year-old man presents with 2 weeks of exertional dyspnea. Pertinent medical history includes hypertension, nephrolithiasis, and internal hemorrhoids. He takes no medications and has no known drug allergies. His father died after a myocardial infarction at 57 years of age. He formerly smoked 1 pack of cigarettes daily for 15 years but ceased tobacco use 10 years before presentation. He ingests 2 glasses of alcohol weekly and denies illicit drug use. His caffeine intake is limited. He is an architect and is married, with healthy children.

On physical examination, his temperature is 98.0°F, blood pressure is 130/85 mm Hg bilaterally, pulse is irregular at 130 beats per minute, and respiratory rate is 18 breaths per minute with an oxygen saturation of 97% while breathing room air. He is a slender white man in no distress. His jugular venous pressure is elevated at 14 cm H2O. There is no thyromegaly, and the carotid upstrokes are brisk, without bruits. Cardiovascular examination reveals a rapid and irregular heart rhythm with variation in the intensity of the first heart sound. The point of maximal impulse is not displaced. The remainder of the chest and abdominal examination is within normal limits. The extremities are warm and show mild pitting edema. Laboratory testing is significant for normal renal function and electrolytes, but a hemogram reveals a mild thrombocytopenia of 90,000 platelets/μL. ECG demonstrates atrial fibrillation (AF) with an average ventricular rate of 123 bpm (Figure 1).

Dr Valentin Fuster: This is a patient with presumably non-valvular AF presenting with a rapid ventricular rate. This is the patient’s first detected episode of AF, and the duration of the arrhythmia, including previously undetected episodes, is unknown. The symptoms of AF may be subtle, and patients may become accustomed to limitations in exertional capacity.

An attempt to elucidate common precipitants for AF, including alcohol consumption, emotional or physical stress, and sleep deprivation, is imperative. Physical examination in this patient suggests congestive heart failure with jugular venous distension and pitting edema. The ECG demonstrates the absence of organized atrial activity and corroborates the physical examination finding of an irregular ventricular rhythm.

Initially, the priority is to address the presenting problem and control the patient’s heart rate. This can be accomplished with β-blockade, which should be initiated in low doses and with careful monitoring given the risk of subsequent exacerbation of heart failure in patients with severe ventricular dysfunction. Although nondihydropyridine calcium channel antagonists could also be effective, they have negative inotropic effects and are better avoided in patients with heart failure. Digoxin, with its positive inotropic effects, is useful in controlling the resting heart rate during AF in the setting of heart failure or hypotension, particularly in combination with β-blockade. However, its relatively slow onset time makes digoxin less effective for acute heart rate control, and its proarrhythmic potential and ineffectiveness in the setting of high sympathetic tone render it less useful as monotherapy. Amiodarone can be used as an additional rate control agent, but given the chance of cardioversion, it should be preceded by at least 3 weeks of therapeutic anticoagulation or imaging to rule out intracardiac thrombus (Figure 2). Long-term, lenient control of the heart rate in AF is easy to achieve and may be sufficient in many patients, but few patients with heart failure have been studied with this strategy, and strict heart rate control is mandatory for patients with tachycardia-related ventricular dysfunction.

After ventricular rate control has been achieved, electric cardioversion should be attempted. The merits of rhythm or rate control aside, when AF is first discovered, I usually recommend an attempt at restoration of sinus rhythm, which may avert the progressive electric and structural remodeling that will ultimately make long-term maintenance of sinus rhythm difficult. Importantly, cardioversion should be delayed until the patient’s volume status is improved, or early AF recurrence will be likely. Because the patient’s AF duration is uncertain, transesophageal echocardiography before cardioversion is

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imperative to exclude a potential cardiogenic thromboembolic source. Echocardiography will also confirm the suspicion for cardiomyopathy and offer insight into the duration, cause, and certain comorbidities associated with AF through evaluation of atrial sizes, ventricular dimensions, wall thickness, valve function, and wall motion.

After successful control of the patient’s heart rate with low-dose metoprolol and improvement in the volume status with diuresis, further investigation followed. The patient’s thyroid studies were within normal limits. Transthoracic echocardiogram demonstrated severe global left ventricular systolic dysfunction with a left ventricular ejection fraction of 10% and mild left ventricular dilatation with an end-diastolic internal diameter of 5.4 cm. There was mild mitral, tricuspid, and aortic valvular insufficiency, as well as mild left atrial dilatation (diameter 4.2 cm; Figure 3A and 3B; associated movies in the online-only Data Supplement). Transesophageal echocardiography corroborated these findings and excluded intracardiac thrombus. The patient underwent direct current cardioversion with restoration of sinus rhythm. Subsequently, exercise stress testing was performed, during which he achieved 12 metabolic equivalents of task (METS) on the Bruce protocol, and myocardial perfusion imaging did not suggest ischemia. In addition to oral metoprolol, an angiotensin-converting enzyme inhibitor was added to his medical regimen, given the cardiomyopathy.

Figure 1. The 12-lead ECG showing atrial fibrillation with a rapid ventricular rate.

Figure 2. Treatment algorithms for the management of paroxysmal or persistent atrial fibrillation in patients with and without heart failure, based on American College of Cardiology/American Heart Association guidelines. AV indicates atrioventricular; and CRT, cardiac resynchronization therapy. *Digoxin may be less effective for acute rate control because of its slower onset of action relative to the other agents, and its effectiveness as monotherapy is limited in the setting of high adrenergic states such as decompensated heart failure. †Dronedarone may not be appropriate for patients with persistent atrial fibrillation. ‡β-Blockers should be administered with caution in patients with heart failure and should be avoided or used with caution in patients who have recently required inotropic support. Metoprolol succinate may be more effective for controlling rapid heart rates associated with atrial fibrillation, but carvedilol has demonstrated greater long-term improvements in heart failure outcomes. §Patients with QRS prolongation and severe systolic dysfunction may benefit from CRT after AV node ablation. ‖The recent European Society of Cardiology guideline update suggests that catheter ablation is a reasonable primary antiarrhythmic strategy in patients who develop heart failure due to atrial fibrillation. Figure adapted from Fuster et al.1
Dr Fuster: Echocardiography demonstrates left ventricular systolic dysfunction and only mild cardiac chamber dilatation, which suggests a relatively acute process. Heart failure may be a consequence or cause of AF; it is crucial to make this distinction. Over time, a persistently elevated ventricular rate can produce a tachycardia-induced cardiomyopathy. However, this entity is a diagnosis of exclusion, and the patient must be investigated for other potential causes of heart failure before one settles on this diagnosis. Generally, tachycardia-induced cardiomyopathy is reversible with adequate ventricular rate control. The cardioversion may be diagnostically helpful, because tachycardia-induced cardiomyopathy may be presumed if the ventricular function improves completely after restoration of sinus rhythm.

Now that the patient is in sinus rhythm, a diagnostic workup should be performed to exclude secondary causes of AF and heart failure. The potential causes of cardiomyopathy in this patient include tachycardia, myocarditis, myocardial ischemia, endocrine dysfunction such as hypothyroidism, substance-related effects, or other more rare infectious or infiltrative diseases. Although in many cases the cause cannot be found, workup for a potentially reversible mechanism is critical. Thyroid function should be evaluated, and exercise stress testing can help exclude ischemia and may additionally be able to reproduce exercise-induced AF. Invasive coronary angiography may be preferred in the evaluation of new-onset heart failure in patients who present with chest pain, or when an ischemic origin is otherwise suspected. Cardiac magnetic resonance imaging may also be a useful diagnostic modality in a patient such as this, because it provides information regarding the underlying cause of the cardiomyopathy. Certain diagnoses such as myocarditis and prior myocardial infarctions are associated with scarring on delayed-enhancement cardiac magnetic resonance imaging, whereas a tachycardia-related cardiomyopathy is typically free of myocardial fibrosis. The absence of delayed enhancement on cardiac magnetic resonance imaging may also suggest potential reversibility of left ventricular dysfunction, which cannot be reliably predicted on the basis of the echocardiographic findings. In addition, dedicated pharmacological stress cardiac magnetic resonance imaging may be used to evaluate for ischemia by assessing myocardial perfusion and wall motion, providing a comprehensive diagnostic option in the workup of this cardiomyopathy.

Despite the patient’s tendency toward minor bleeding with internal hemorrhoids and a baseline thrombocytopenia, he was prescribed subcutaneous low-molecular-weight heparin as a bridge to long-term warfarin therapy for stroke prevention.

Dr Fuster: In any patient who is cardioverted, anticoagulation is mandatory for at least 4 weeks because of a high risk for early thromboembolism resulting from transient atrial stunning. Thereafter, the first step in determining the appropriateness for long-term anticoagulation is to stratify the patient’s thromboembolic risk. Even if sinus rhythm is restored, the need for anticoagulation is determined on the basis of the baseline stroke risk. Traditionally, the CHADS2 scoring scheme has been used to estimate the risk of stroke by assigning points for the following risk factors: Congestive...
heart failure (1 point), hypertension (1 point), age >75 years (1 point), diabetes mellitus (1 point), and prior stroke or transient ischemic attack (2 points). With hypertension and congestive heart failure, this patient has a CHADS$_2$ score of 2, which indicates a high risk for thromboembolism and argues in favor of anticoagulation. Congestive heart failure alone, in my opinion, is a compelling indication for anticoagulation. The CHA$_2$DS$_2$VASc score, which expands on CHADS$_2$ by assigning 1 point for age ≥65 years (and 2 points for age ≥75 years) and 1 point each for vascular disease (prior myocardial infarction, complex aortic plaque, or symptomatic peripheral arterial disease) and female sex is a newer risk scheme that appears to outperform the CHADS$_2$ model in identifying patients at the lowest risk of thromboembolism. Once stroke risk is estimated, the patient’s bleeding risk with anticoagulation therapy should also be considered. The HAS-BLED score (which assigns points for hypertension, abnormal renal and hepatic function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly age, and concomitant drug or alcohol use) may be helpful in this regard; a HAS-BLED score ≥3 represents a high risk for bleeding and indicates the need for careful monitoring when anticoagulation is used (Table 1).$^{3–5}$

Clinical decision making can be challenging when using these risk schema, however, because there is substantial overlap between risk factors for thromboembolism and conditions that increase bleeding risk. Recent analyses suggest that the thromboembolic risk is much greater than the risk of bleeding in most patients, except perhaps in a small subset of patients at extremely high bleeding risk, such as those with prior episodes of major bleeding or malignant hypertension. Anticoagulation is therefore indicated in the majority of patients with AF and should be deferred only in those at very low risk for thromboembolism or prohibitively high risk for bleeding. For patients with both a prohibitively high risk of bleeding and a very high risk of stroke, one may consider a mechanical alternative to anticoagulation for stroke prevention, such as surgical or percutaneous left atrial appendage ligation or the Watchman left atrial appendage occlusion device. The percutaneously implanted Watchman device has shown promise in reducing stroke risk to a similar degree as anticoagulation with warfarin; however, long-term experience is lacking. Anticoagulation is still recommended after Watchman implantation for at least the short-term, and these devices have not yet been approved by the Food and Drug Administration.

The era of stroke prevention in AF is quickly evolving, with new agents such as the direct thrombin inhibitor dabigatran and the factor Xa inhibitors apixaban and rivaroxaban. These novel anticoagulant agents may be given without the need for coagulation monitoring, offering an appealing alternative to warfarin. In this patient, however, I am inclined to use warfarin, an agent with which I have more experience. In particular relevance to this case, there are no data on the use of dabigatran in patients with AF and very low ejection fractions.

The patient was discharged home in sinus rhythm but presented to the emergency department within 1 week with recurrent rapid AF. He had been compliant with his medical regimen before this presentation and was warm and euvelomic on physical examination. Amiodarone was initiated, and the next day another electric cardioversion was performed, again restoring sinus rhythm. After completion of intravenous and subsequently oral loading, amiodarone was continued as oral maintenance therapy. Repeat transthoracic echocardiography performed 1 month after initial presentation revealed recovery of systolic function, with a left ventricular ejection fraction of 60% (Figures 3C and 3D; associated movies in the online-only Data Supplement). He subsequently remained free of cardiac symptoms for >2 years, and surveillance 24-hour Holter monitoring performed 3 and 12 months after cardioversion revealed no evidence of recurrent atrial fibrillation.

Dr Fuster: With the information regarding the recovery of systolic function now available, a tachycardia-induced cardiomyopathy appears likely. This suggests that the AF had been ongoing for some time before diagnosis. Given the patient’s early recurrence and disabling symptoms, I agree that another attempt at restoration of sinus rhythm with electric cardioversion preceded by the addition of an antiarrhythmic drug is warranted. However, antiarrhythmic drug therapy is frequently limited by suboptimal efficacy, poor tolerability, and proarrhythmic potential. In the setting of this patient’s heart failure, the options are limited to amiodarone and dofetilide as first-choice antiarrhythmic agents. Dofetilide requires careful monitoring for QT prolongation, which may result in torsade de pointes and sudden death. Vaughan Williams class IA and IC antiarrhythmic drugs increase the risk for sudden death in patients with structural heart disease, and dronedarone has also demonstrated adverse outcomes in patients with New York Heart Association class II to IV symptoms or recently

### Table 1. Stroke or Thromboembolism Rates Based on CHADS2 and CHA2DS2VASc Scores and Bleeding Rates Based on HAS-BLED Score

<table>
<thead>
<tr>
<th>CHADS$_2$ Score</th>
<th>Adjusted Stroke Rate, %/y$^*$</th>
<th>CHA2DS2VASc Score</th>
<th>Adjusted Thromboembolism Rate, %/y$^+$</th>
<th>HAS-BLED Score</th>
<th>Major Bleeding Rate, %/y$^+$</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>1.9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>2.9</td>
<td>1</td>
<td>1.3</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>2</td>
<td>4.0</td>
<td>2</td>
<td>2.2</td>
<td>2</td>
<td>2.2</td>
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</tr>
<tr>
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<td>8.5</td>
<td>4</td>
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</tr>
<tr>
<td>5</td>
<td>12.5</td>
<td>5</td>
<td>6.7</td>
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<td>8</td>
<td>6.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>15.2</td>
<td>9</td>
<td>15.2</td>
<td></td>
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</tr>
</tbody>
</table>

CHADS$_2$ indicates congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke (2 points); CHA2DS2VASc, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, stroke (2 points), vascular disease, age ≥65 years, sex category (ie, female sex); and HAS-BLED, hypertension, abnormal renal or liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly (age ≥75 years), drug/alcohol use concomitantly.

$^*$Data from Gage et al.$^3$

$^+$Data from Lip et al.$^4$

$^+$Stroke rates are adjusted for warfarin use.

$^+$Data from Gallego et al.$^5$. 

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*Dr Fuster: With the information regarding the recovery of systolic function now available, a tachycardia-induced cardiomyopathy appears likely. This suggests that the AF had been ongoing for some time before diagnosis. Given the patient’s early recurrence and disabling symptoms, I agree that another attempt at restoration of sinus rhythm with electric cardioversion preceded by the addition of an antiarrhythmic drug is warranted. However, antiarrhythmic drug therapy is frequently limited by suboptimal efficacy, poor tolerability, and proarrhythmic potential. In the setting of this patient’s heart failure, the options are limited to amiodarone and dofetilide as first-choice antiarrhythmic agents. Dofetilide requires careful monitoring for QT prolongation, which may result in torsade de pointes and sudden death. Vaughan Williams class IA and IC antiarrhythmic drugs increase the risk for sudden death in patients with structural heart disease, and dronedarone has also demonstrated adverse outcomes in patients with New York Heart Association class II to IV symptoms or recently...*
decompensated heart failure. I would initiate amiodarone, which is relatively effective and carries less proarrhythmic risk. The clinician must be alert to the various drug-drug interactions and potential extracardiac toxicities of amiodarone, which include pulmonary fibrosis, bradycardia, hepatic toxicity, thyroid dysfunction, and ophthalmologic complications. I am thus hesitant to continue amiodarone for long-term maintenance therapy, especially now that systolic function has improved and little is known about the natural history of the patient’s AF. It is preferable to discontinue amiodarone after some time and monitor for arrhythmia recurrence.

Fewer than 3 years after presentation, the patient began experiencing symptomatic AF with increasing frequency and duration. He developed unexplained weight loss, heat intolerance, and nervousness. Laboratory testing demonstrated a depressed serum thyroid-stimulating hormone at <0.01 mIU/L and an elevated free thyroxine level at 4.3 ng/mL. After discontinuation of amiodarone, the patient’s thyroid function normalized; however, paroxysms of AF continued.

Dr Fuster: I am not surprised about the recurrence, or regarding the development of amiodarone toxicity. AF is a chronic disorder in which recurrence is common. Although amiodarone can suppress AF and control symptoms in many patients, adverse effects occur commonly in patients treated with this agent long-term. In this patient with no prior history of thyroid disease, the development of hyperthyroidism can be attributed to the toxic effects of amiodarone, and workup is indicated to implicate the type of amiodarone-induced thyrotoxicosis involved, which will then guide further management. Systemic symptoms are not uncommon with amiodarone-related hyperthyroidism, and in fact, the reoccurrence of AF, which had previously been controlled, can also suggest the diagnosis. There are other options for treatment in this case, and amiodarone should be promptly discontinued.

In the current landscape, which has evolved dramatically over the past few years, more effective options are available for rhythm control, namely, catheter-guided ablation predicated on electric isolation of AF triggers within the pulmonary veins. With long-term data regarding the success of ablation now available, I would strongly consider this approach. On the other hand, it is reasonable to consider a trial of a different antiarrhythmic agent, although this strategy is less likely to successfully restore sinus rhythm. Dronedarone could be considered in this relatively young patient with normal ventricular function and limited comorbidities. Although initially touted as being a safer alternative to amiodarone, recent data suggest that dronedarone is less effective and may be associated with harm in patients with symptomatic heart failure and older patients with persistent AF. Because the patient’s left ventricular function has normalized, he is a candidate for class IC antiarrhythmic agents, such as flecainide and propafenone. If this class of agents is used, concomitant β-blocker therapy is necessary to prevent rapid atrioventricular conduction in a more organized atrial arrhythmia.

The patient was treated with dronedarone and subsequently flecainide. However, he continued to experience frequent palpitation, which interfered with his daily activities and dramatically affected his quality of life. He eventually progressed to persistent AF.

Dr Fuster: At this point, ablation must be considered, because it is the most likely means to successfully restore sinus rhythm and control this patient’s symptoms. Data from international registries have demonstrated that ablation is successful in maintaining sinus rhythm in 85% and 72% of patients with paroxysmal and persistent AF, respectively, at 3 years of follow-up. This does not include recurrences that develop within the first few months after ablation, which are often transient and should not be considered procedural failures. Factors that have been associated with a worse outcome after AF ablation include nonparoxysmal AF, sleep apnea, obesity, increased left atrial size, older age, hypertension, and left atrial fibrosis as detected by cardiac magnetic resonance imaging. In this patient, I believe the likelihood of maintaining sinus rhythm after ablation is good, particularly if ablation is pursued early, before AF becomes more persistent. Importantly, recent nonrandomized retrospective studies have also demonstrated that successful restoration of sinus rhythm with ablation may reduce AF-related mortality and stroke risk. Although these potential benefits have not yet been proven, ablation is being considered early in the treatment course for many patients. However, clinicians should be careful not to refer for ablation immediately after a first diagnosed episode of AF. There is a minority of patients who experience only a single episode of AF in their lifetime, often in the setting of a reversible precipitant such as a viral illness or recent alcohol use. It would be a mistake to send these patients for a potentially complicated procedure without recognizing and addressing the underlying triggers.

The patient underwent ablation for AF. Electrical isolation of the pulmonary veins was created with radiofrequency energy delivery, which led to immediate restoration of normal sinus rhythm (Figure 4). He did well postoperatively and reported no symptomatic arrhythmia recurrence at outpatient follow-up several months later. During this visit, he asked whether he could discontinue anticoagulation therapy.

Dr Fuster: After ablation, it is mandatory to monitor for recurrent arrhythmia. Discontinuation of anticoagulation therapy may be reasonable after successful ablation, especially in patients with a low risk for thromboembolism. Although risk factor control has not been proven to modify long-term stroke risk in patients with AF, if normal blood pressure is now restored with antihypertensive medication, this patient effectively has zero active CHA2DS2-VASc risk factors. Therefore, even if he has recurrences of AF, I might feel comfortable using aspirin for stroke prevention. Otherwise, I would discuss it with the patient and would continue anticoagulation therapy if he were willing. But this conversation is premature, and we must first evaluate for recurrent postablation arrhythmias with serial ambulatory monitoring. If international registry findings that suggest a reduction in stroke risk after AF ablation are validated in prospective studies, there would be sound rationale for stopping anticoagulation after successful
ablation. For now, this should be done only when the patient-specific stroke risk is low.

Although the patient remained free of symptomatic arrhythmia for 2 years after the ablation, he eventually returned with palpitation, lightheadedness, and polyuria. ECG demonstrated atrial flutter with an average ventricular rate of 115 bpm (Figure 5). Despite ventricular rate control, he remained symptomatic.

Dr Fuster: The ECG now demonstrates atrial flutter. Interestingly, polyuria may be a symptom of atrial arrhythmias as a result of tachycardia-induced diuresis and natriuresis. In patients with AF, other atrial arrhythmias are common and may arise de novo or as a result of conduction delay created during ablation. This is another reason why careful monitoring for recurrent arrhythmias is critical before anticoagulation is stopped. If typical cavotricuspid isthmus-dependent atrial flutter is seen, catheter ablation in the right atrium is likely to be successful in eliminating this arrhythmia, with little procedural risk. A strategy of cardioversion followed by active monitoring may also be considered, but recurrence is likely without reintiation of antiarrhythmic drugs. Furthermore, iatrogenic arrhythmias resulting from radiofrequency ablation in the left atrium are frequently persistent and difficult to control with medications alone. Atrial tachycardias that arise after AF ablation are often associated with rapid ventricular rates and may thereby cause even more severe symptoms than did the AF for which ablation was initially indicated. Given this patient’s symptoms, I would again offer him an electrophysiological study and targeted ablation.

The patient underwent electrophysiological study, which revealed typical atrial flutter. Radiofrequency ablation was performed along the cavotricuspid isthmus, with resultant restoration of sinus rhythm. He has thereafter remained asymptomatic.

Discussion

AF and heart failure frequently coexist, and when they present concomitantly, they involve unique prognostic and management considerations (Figure 2). Although decompensated heart failure can trigger an acute AF episode, AF is also a frequent cause of heart failure decompensation and is an independent risk factor for morbidity and mortality among patients with heart failure. AF itself, even when asymptomatic, may lead to progressive cardiac failure, because rapid ventricular heart rates may induce reversible structural and cellular changes that result in ventricular dysfunction, chamber dilation, and congestive heart failure. At least one quarter of patients with AF and left ventricular dysfunction have some degree of tachycardia-induced ventricular impairment. The diagnosis of tachycardia-induced cardiomyopathy cannot be
made, however, until the ventricular function improves after rhythm or rate control.

The decision to pursue restoration of sinus rhythm in patients with heart failure and concomitant AF is driven by the severity of AF-related symptoms and hemodynamic intolerance. Rhythm control strategies based on antiarrhythmic medications have not demonstrated improvements in mortality, stroke, or hospitalization rates compared with rate control in randomized trials such as the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) or Rate Control Versus Electrical Cardioversion for Persistent Atrial Fibrillation (RACE). In patients with heart failure, despite the contribution of AF to adverse outcomes, comparative studies have similarly found no advantage with pharmacological rhythm control. However, effective rhythm strategies that avoid antiarrhythmic drug-related toxicity may still improve outcomes in selected patients. Accordingly, a post hoc analysis of AFFIRM found successful restoration of sinus rhythm, independent of antiarrhythmic medication use, to be associated with a substantially lower risk of death. Furthermore, nonblinded studies have suggested that AF ablation may improve left ventricular ejection fraction and functional capacity more than rate control in patients with heart failure. Additionally, restoration of sinus rhythm is often preferred in patients with tachycardia-induced cardiomyopathy to prevent transient exacerbations of tachycardia that may acutely worsen ventricular function. Antiarrhythmic drugs improve the chances of maintaining sinus rhythm, but safety considerations limit options in patients with heart failure to Vaughan Williams class III agents. Amiodarone is the most effective antiarrhythmic drug for preventing AF recurrence and has limited proarrhythmic toxicity, but AF-related symptoms should be onerous enough to justify the substantial extracardiac risks associated with long-term treatment. Thyroid dysfunction, ranging from immediate laboratory test abnormalities to overt hypothyroidism and hyperthyroidism, occurs in 10% of amiodarone-treated patients, and guidelines recommend monitoring thyroid function tests every 6 months. Hyperthyroidism in amiodarone-treated patients is categorized into 2 subtypes of thyrotoxicosis. In type 1 amiodarone-induced thyrotoxicosis, which typically occurs in patients with underlying thyroid pathology and is more prevalent in iodine-depleted geographic areas, the iodine load caused by chronic amiodarone treatment results in excessive production of thyroid hormones. Type 2 toxicity, a form of thyroiditis in which amiodarone causes destruction of thyroid follicular cells, is more common in Western countries and typically occurs in patients with normal thyroid glands. Distinction between the 2 subtypes is important to guide therapy. In type 1 amiodarone-induced thyrotoxicosis, preexistent thyroid pathology is frequently identified by history and physical examination, and sonography reveals an enlarged gland or nodular goiter with increased vascularity on color Doppler. In contrast, patients with type 2 toxicity often have no demonstrable thyroid pathology. Treatment includes discontinuation of amiodarone in both subtypes when possible. Patients with type 1 toxicity may require high doses of antithyroid drugs, whereas type 2 can be effectively treated with oral prednisone. Patients with mild type 2 thyrotoxicosis often have spontaneous resolution after amiodarone is withdrawn; because of its long half-life, however, thyroid abnormalities may persist for months thereafter.

Catheter ablation for AF has demonstrated greater efficacy in maintaining sinus rhythm and greater improvements in symptom severity and quality of life than have antiarrhythmic medications, but only recently have long-term data assessing the success of modern AF ablation become available. In an international registry of 1273 patients who underwent AF ablation, successful maintenance of sinus rhythm was achieved in 85% of patients with paroxysmal and 72% with persistent AF (76% and 60% not taking antiarrhythmic medications, respectively) at a mean follow-up of 3.1 years. In patients who do not have a recurrence in the first year after ablation, very late recurrence (up to 5 years) develops in <9% of patients. Importantly, however, a second procedure may be necessary after ablation, particularly in patients with persistent AF; attributable to incomplete lines of conduction block that may permit AF to recur or create substrate for novel reentrant left atrial arrhythmias. Additionally, atrial flutter is commonly coexistent in patients with AF and can present even after successful pulmonary vein isolation. Nevertheless, the superiority of ablation over antiarrhythmic drugs in maintaining sinus rhythm has resulted in expert recommendations for earlier implementation of ablation after failure of drug therapy in symptomatic patients, with consideration of ablation as a first-line option in cases when success is most likely (Table 2).

Whether durable restoration of sinus rhythm after AF ablation, without the long-term toxicity associated with antiarrhythmic drugs, can translate into improved survival and stroke rates has not been proven. However, in a nonrandomized registry, rates of death and stroke in patients who underwent ablation were significantly lower than in a separate cohort of patients with medically managed AF and were reduced to levels similar to those in a matched cohort of patients without AF. Maintenance of sinus rhythm achieved with ablation is associated with better outcomes, but it is not known whether

| Table 2. Consensus Indications for Catheter Ablation of Atrial Fibrillation, Produced by the Heart Rhythm Society and the European Heart Rhythm Association |

<table>
<thead>
<tr>
<th>Indications for Catheter Ablation of AF</th>
<th>Class</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic AF refractory or intolerant to at least 1 class 1 or class 3 antiarrhythmic medication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal AF: Catheter ablation is recommended*</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Persistent AF: Catheter ablation is reasonable</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Longstanding persistent AF: Catheter ablation may be considered</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Symptomatic AF before initiation of antiarrhythmic drug therapy with a class 1 or class 3 antiarrhythmic agent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal AF: Catheter ablation is reasonable</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Persistent AF: Catheter ablation may be considered</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Longstanding persistent AF: Catheter ablation may be considered</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; and LOE, level of evidence.
*When performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced center.

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this association is causative. Results from ongoing studies such as the Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation Trial (CABANA) are needed to evaluate the long-term effects of ablation with regard to mortality, stroke risk, progression of AF, and heart failure.23,25 Nevertheless, the preliminary registry data have important implications regarding anticoagulation management in patients who remain in sinus rhythm after ablation. Retrospective studies with follow-up over 3 years have demonstrated low rates of thromboembolism in patients in whom anticoagulation was stopped after successful ablation, even in the presence of high CHADS2 scores.26,27 However, thorough monitoring for arrhythmia recurrence is necessary before cessation of antithrombotic therapy can be considered, because asymptomatic recurrences and the development of new atrial arrhythmias after ablation are not uncommon.22 Recent consensus recommendations advise further anticoagulation in patients with a CHADS2 score ≥2 after successful ablation, with more flexibility in patients at lower stroke risk.23

In summary, AF is a chronic disease associated with increased mortality and morbidity, particularly in patients with heart failure. Antiarrhythmic medications may control the arrhythmia, but carry substantial risk of toxicity. However, in well-selected patients, the benefits of restoring sinus rhythm should not be overlooked, and a more invasive strategy may be justified, particularly when symptoms are intolerable.

Disclosures

None.

References


Key Words: antiarrhythmia agents ■ anticoagulants ■ atrial fibrillation ■ catheter ablation ■ heart failure ■ stroke ■ tachyarrhythmias
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