Catheter Ablation for Atrial Fibrillation

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A 59-year-old man with hypertension and diabetes presents with palpitations, fatigue, and shortness of breath and is found to be in atrial fibrillation. He has had recurring episodes of atrial fibrillation over the previous 5 years, typically with similar symptoms, and has received warfarin for stroke prevention. He has required direct-current cardioversion to restore sinus rhythm on two occasions despite treatment with flecainide and subsequently with dofetilide. The use of amiodarone resulted in hyperthyroidism. After undergoing cardioversion, he is referred to a cardiac electrophysiologist, who recommends catheter ablation.

THE CLINICAL PROBLEM

Atrial fibrillation affects up to 5 million people in the United States, and data suggest that as the population ages, the incidence will continue to increase.¹,² The rate of ischemic stroke among patients with nonvalvular atrial fibrillation averages 5% per year.³ The rate of death among patients with atrial fibrillation is about double that among patients with normal sinus rhythm.³ The overall cost of treating recurrent atrial fibrillation has been estimated to be more than $6.5 billion per year.⁴ Atrial fibrillation is usually a progressive disease. The natural history often begins with infrequent episodes of limited duration termed paroxysmal atrial fibrillation (often defined as episodes that terminate spontaneously within 1 week). Such episodes then tend to become more frequent and longer in duration, progressing to persistent atrial fibrillation (which fails to terminate spontaneously within 7 days and may require cardioversion) or permanent atrial fibrillation (if the arrhythmia lasts for more than 1 year and cardioversion either has not been attempted or has failed). Symptoms include palpitations, shortness of breath, and fatigue; particularly for symptomatic patients, atrial fibrillation has adverse effects on quality of life.³

PATHOPHYSIOLOGY AND EFFECT OF THERAPY

The electrophysiological basis of atrial fibrillation requires both a trigger that initiates the dysrhythmia and a substrate that can sustain it.⁵,⁶ The most common triggers of atrial fibrillation are ectopic atrial beats that arise from the muscle sleeves of the pulmonary veins.⁷,⁸ These triggers may be provoked by the intrinsic activity of cardiac ganglionic plexuses, which are clustered in the vicinity of the pulmonary vein–left atrial junction.⁹,¹⁰ The pulmonary vein–left atrial junction and an enlarged atrium harboring fibrosis and inflammation serve as the substrate for sustaining wavelets of atrial fibrillation. With persistence of atrial fibrillation, a further electrophysiological change in the atria — namely, shortening of the refractory period...
of the atrial muscle — occurs and predisposes to the development of other triggers and wavelets. This process results in perpetuation of atrial fibrillation and in a greater predisposition to atrial fibrillation. Maintenance of sinus rhythm can reverse these changes and mechanisms. Hence, atrial fibrillation begets atrial fibrillation, and sinus rhythm begets sinus rhythm.11-13

Atrial fibrillation ablation is a therapeutic technique that uses radiofrequency energy or freezing to destroy atrial tissue that is involved in the propagation of the dysrythmia. Radiofrequency ablation generates an alternating electrical current that passes through myocardial tissue, creating heat energy that conducts to deeper tissue layers. At temperatures of 50°C or higher, most tissues undergo irreversible coagulation necrosis and then evolve into nonconducting myocardial scar tissue.14,15 Cryoablation destroys tissue by freezing.

The principal objective of atrial fibrillation ablation is the electrical disconnection of the pulmonary-vein triggers from the atrial substrate (often called “pulmonary-vein isolation”).16,17 To achieve this goal, ablation is performed around the pulmonary-vein orifice (Fig. 1 and 2). Ablation of sites beyond the pulmonary vein–left atrial junction in the atrial substrate itself, targeting so-called complex fractionated electrograms, is not necessary in paroxysmal atrial fibrillation but may be very important in patients with persistent atrial fibrillation.17

The Food and Drug Administration (FDA) has approved both radiofrequency ablation and cryoablation for clinical use in patients with paroxysmal atrial fibrillation. Ablation procedures are also performed in patients with persistent or permanent atrial fibrillation, although such use is not FDA-approved and is considered off-label.
Several randomized trials have shown superior outcomes for radiofrequency ablation as compared with antiarrhythmic drug therapy. For example, in one trial, 198 patients with paroxysmal atrial fibrillation in whom antiarrhythmic drug therapy had previously failed were randomly assigned to either radiofrequency ablation or antiarrhythmic drug therapy with other agents. Patients assigned to catheter ablation received antiarrhythmic drug therapy for the first 6 weeks after treatment, and recurrences during this interval were not included in the primary trial end point (a so-called blanking period to allow healing of the atrial myocardium after the procedure). At 1 year, 86% of the patients assigned to catheter ablation and 22% of those assigned to antiarrhythmic drug therapy had not had a recurrent atrial tachyarrhythmia (P<0.001). Hospitalizations for cardiovascular disease were also less frequent in the ablation group.

In another trial, 167 patients with drug-resistant paroxysmal atrial fibrillation were randomly assigned to ablation or another antiarrhythmic drug. At 9 months, 63% of the patients assigned to catheter ablation and 17% of those assigned to antiarrhythmic drug therapy were free of recurrent atrial tachyarrhythmias. Patients in the ablation group also had significantly greater improvement in quality of life.

Cryoablation has also been shown to be effective, although the results of the principal randomized trial of this technique, Sustained Treatment of Paroxysmal Atrial Fibrillation (STOP AF; ClinicalTrials.gov number, NCT00523978), have not yet been published. In the STOP AF trial, 245 patients with paroxysmal atrial fibrillation in whom previous antiarrhythmic drug therapy had failed were randomly assigned to treatment with a cryoablation balloon or antiarrhythmic drugs. One year after treatment, 69.9% of the patients treated with cryoablation had no detectable atrial fibrillation, as compared with 7.3% of those who were treated with antiarrhythmic medications.

An important limitation of the evidence is that atrial fibrillation ablation has not yet been studied for its potential impact on important clinical outcomes such as the rates of death, stroke, heart failure, or health care utilization.

**Clinical Use**

Management of atrial fibrillation hinges on decreasing the risk of stroke, preventing the development of heart failure, and relieving symptoms. For some patients, maintenance of sinus rhythm is not essential, and indeed, a strategy of attempting to maintain sinus rhythm specifically with antiarrhythmic drugs has not been shown to reduce mortality. However, some patients remain very symptomatic while in atrial fibrillation, despite rate control, and for such patients a rhythm-control approach may be preferable.

Antiarrhythmic drugs are considered the first-line treatment for maintenance of sinus rhythm. However, the efficacy of these agents is not favorable, with only 50% of patients so treated maintaining sinus rhythm after 1 year of follow-up. In addition, the side effects of antiarrhythmic drugs are not trivial. In a recent meta-analysis, these side effects included treatment-related death in 0.5% of patients, torsades de pointes in 0.7%, neuropathy in 5.0%, and thyroid dysfunction in 3.3%. Less serious side effects such as gastrointestinal symptoms occur more frequently and may have a substantial effect on quality of life.

Catheter ablation is indicated to prevent the recurrence of symptomatic atrial fibrillation in patients who have had recurrent episodes of atrial fibrillation despite continuous antiarrhythmic drug therapy. Catheter ablation may be considered for patients with drug-refractory paroxysmal atrial fibrillation who can tolerate the procedure and for patients with atrial flutter who have failed antiarrhythmic drug therapy. Catheter ablation is also indicated for patients who have had recurrent atrial fibrillation despite antiarrhythmic drug therapy and for patients with atrial fibrillation who require sinus rhythm for atrioventricular node reentry tachycardia.

Before ablation and after ablation, electrographic recordings of electrocardiographic leads I and V, and from electrodes positioned within the atrium (L1–2 through L10–11), in the proximal and distal coronary sinus (CS, and CS, and on the ablation catheter itself (Abl d) are shown. Stimuli to initiate atrial depolarizations are administered through a stimulating electrode (STIM). Arrows point to pulmonary-vein potentials recorded with the use of a circular mapping catheter. These potentials are present before ablation but disappear after ablation, indicating that pulmonary vein–left atrial electrical disconnection and pulmonary-vein isolation have been achieved.
patients in whom medical therapy has been ineffective. It is important to note that most randomized studies included only patients with paroxysmal atrial fibrillation and that the FDA has approved catheters for use only in such patients. However, ablation of persistent or permanent atrial fibrillation in symptomatic patients in whom medical therapy has failed is reasonable, since such patients have been shown to have considerable symptom relief with a successful ablation. Ablation is most effective in patients with paroxysmal atrial fibrillation and less effective in patients with persistent atrial fibrillation, heart failure, or valvular disease. The desire to discontinue oral anticoagulation by itself is not a valid indication to refer a patient for atrial fibrillation ablation. The presence of a left atrial thrombus is a contraindication to catheter ablation, and all patients who present in atrial fibrillation should have either clear documentation of therapeutic anticoagulation for at least 6 weeks before the procedure or a transesophageal echocardiogram showing that no thrombus is present.

Ablation may be performed while the patient is under intravenous conscious sedation or general anesthesia. Access to the pulmonary veins in the left atrium is achieved by inserting sheaths into the femoral veins and advancing catheters to the inferior vena cava and right atrium, and then crossing the interatrial septum by transseptal puncture with a specially designed needle. Heparin is administered for prevention of thrombosis either just before or just after transseptal puncture.

The procedure is performed with the use of fluoroscopy and, in some cases, with guidance from electroanatomical mapping (a tool that uses a specialized recording catheter with location sensors to create a three-dimensional anatomical reconstruction of the left atrium with superimposed electrical activation data) (Fig. 3). Intracardiac echocardiography is used in many laboratories to guide transseptal puncture under direct visualization (Fig. 4) and also to guide pulmonary-vein isolation. With intracardiac echocardiography, it is possible to visualize the antrum of each pulmonary vein and position the catheters for ablation appropriately. It also aids in the early detection of complications such as thrombus formation and pericardial effusion. During radiofrequency ablation, a thermistor probe is inserted through the patient’s nose or mouth into the esophagus to monitor esophageal temperatures; an increase in temperature implies transmission of the heat generated by the procedure into the esophagus with a consequent risk of esophageal injury.

Ablation around the antrum of each pulmonary vein is performed to achieve complete electrical disconnection between the pulmonary vein and left atrium (pulmonary-vein isolation). With radiofrequency ablation, this goal is achieved by the sequential application of radiofrequency energy at a series of individual closely spaced points around the circumference of the vein. With cryoab-
lation, a balloon-tipped catheter is advanced to the antrum of each pulmonary vein and the balloon is inflated to form a seal. The balloon is then filled with coolant, which creates a circumferential zone of tissue necrosis around the vein orifice.

With successful pulmonary-vein isolation, ectopic electrical triggers arising in the pulmonary veins encounter a region of scarring that obstructs the propagation of electrical impulses to the atrium. Isolation is confirmed by the absence of electrograms at the pulmonary vein–left atrial junction or by a reduction in the amplitude of such electrograms, which is usually detected with the use of a circular mapping catheter (Fig. 2). During the procedure, a nonpulmonary-vein trigger (e.g., arising in the body of the left atrium) may be recognized as a contributing cause of atrial fibrillation and is then targeted for ablation. In patients with persistent atrial fibrillation, pulmonary-vein isolation may not be sufficient, and adjunctive ablation of complex fractionated electrograms may be performed elsewhere in the atrium.

Patients are observed overnight and discharged the following morning. After discharge, patients are often treated with an antiarrhythmic drug for 2 or 3 months to minimize early recurrence of atrial fibrillation. Oral anticoagulation should be continued for at least 2 months after ablation.

Patients are provided with event monitors for several months after ablation and are asked to transmit rhythm data weekly and whenever symptoms are reported. The 2007 expert consensus statement on catheter and surgical ablation of atrial fibrillation by the Heart Rhythm Society, the European Heart Rhythm Association, and the European Cardiac Arrhythmia Society (HRS/EHRA/ECAS) recommends 24-hour Holter monitoring every 3 to 6 months for at least 2 years. Recurrence of atrial fibrillation in the first 3 months may be attributable to inflammation and irritation caused by the ablation; the risk of further recurrence typically abates as the inflammation resolves. However, data suggest that recurrences later in this period are associated with long-term recurrence.

Patients should be evaluated within 3 to 4 months to assess the outcome of ablation. During long-term follow-up, one of four possible outcomes may be encountered. Some patients are found to be apparently free of atrial fibrillation, based on both symptoms and rhythm monitoring, even after discontinuation of antiarrhythmic drugs. A second group has recurrent atrial fibrillation that can be controlled with previously ineffective drugs; in such patients, a second ablation can be deferred. A third group of patients has recurrent symptomatic atrial fibrillation despite antiarrhythmic drug therapy; a second ablation is indicated in such patients. Finally, a fourth group of patients has recurrent, but asymptomatic, atrial fibrillation. Such patients can be treated with rate control.

Recurrent atrial fibrillation is common after catheter ablation. One article described outcomes in 831 patients. At 1 year, 633 (76%) were free of arrhythmia, 17 (2%) had recurrence managed with antiarrhythmic drugs, 161 (19%) had recurrence managed with a second ablation, and 20 (2%) had recurrence managed with rate control.

Regardless of the apparent efficacy of ablation, the guidelines recommend that anticoagulation

![Figure 4. Intracardiac Echocardiographic Images.](image-url)

Panel A shows transseptal puncture. The triangular echodensity indicates tenting of the interatrial septum with the transseptal needle (arrow). Panel B shows the interatrial septum, left atrium, and circular mapping catheter in a large common pulmonary vein.
in the long term (after 2 months) should be based on the risk of stroke as predicted by the CHADS\textsuperscript{2} score. The CHADS\textsuperscript{2} score is a risk-prediction score, with values ranging from 0 to 6, that assigns one point each for congestive heart failure, hypertension, age of 75 years or older, and diabetes, and two points for stroke or transient ischemic attack. Typically, therapeutic anticoagulation is recommended for patients with a CHADS\textsuperscript{2} score of 2 or more. The rationale for this approach is that asymptomatic recurrence of atrial fibrillation cannot be ruled out as a possibility, even among patients who have undergone apparently very successful ablation.

In the United States, the initial cost of atrial fibrillation ablation is between $17,000 and $25,000. There is an additional cost of about $1,500 to $2,000 per year thereafter for monitoring and follow-up visits.

### Adverse Effects

A recently published survey reported data on 16,309 patients undergoing atrial fibrillation ablation worldwide, including data on adverse events. Almost all the procedures in this survey were performed with the use of radiofrequency ablation; cryoablation was used in less than 2% of cases. In this survey, the risk of a major complication was 4.5%.\textsuperscript{29} The risk of death was 0.15%.

Cardiac tamponade due to perforation is a potentially life-threatening complication occurring in approximately 1.3% of patients undergoing atrial fibrillation ablation. Cardiac perforation can be secondary to a misdirected transseptal puncture, trauma due to catheter movement, or excessive focal application of radiofrequency energy. Direct injury to the phrenic nerve can also occur as a result of ablation near the right superior pulmonary vein and superior vena cava. Such injury can cause diaphragmatic paralysis. Esophageal injury has been reported in approximately 10% of patients; atrioesophageal fistulas are rare (occurring in 0.04% of patients) but can be devastating and even lethal.

Cerebrovascular thromboembolism has been reported to occur in up to 2% of patients. Thromboembolic complications can arise because of clot or char formation on the sheaths and catheters or at the site of ablation. The diagnosis is usually made during the procedure, but thromboemboli can occur several days later.

Pulmonary-vein stenosis is a late complication of ablation caused by injury to the pulmonary-vein musculature. The reported incidence varies from 0 to 10%. Symptoms of pulmonary-vein stenosis include chest pain, shortness of breath, cough, and recurrent lung infections. The diagnosis is made with the use of computed tomographic imaging or magnetic resonance scanning or by means of ventilation–perfusion lung scanning.

Iatrogenic atypical flutter, a type of regular atrial arrhythmia encountered after ablation, can result from ablation lines that do not completely isolate the pulmonary veins. The occurrence of this complication depends to a large extent on the technique of ablation; the incidence ranges from 1.8 to 14.3%. Other, less frequent, complications are listed in Table 1.\textsuperscript{17,29}

### Areas of Uncertainty

The success of atrial fibrillation ablation is variable, and there is evidence that some of this variation is operator-dependent. High success rates and low complication rates are achieved in high-volume, experienced centers. Furthermore, results from various centers and studies differ greatly because of variations in technique, reporting, and follow-up. Greater standardization of practice is therefore necessary to achieve consistency in clinical outcomes.

The restoration of sinus rhythm by catheter ablation of atrial fibrillation improves quality of life and may improve the left ventricular ejection fraction in patients with heart failure. However, the long-term effect of this procedure requires further study; this is especially true in patients with persistent, long-standing atrial fibrillation and enlarged atria. In addition, the durability of maintenance of sinus rhythm after ablation in the long term is unknown. Preliminary data suggest that the recurrence rate after the first year is 6 to 9% per year.\textsuperscript{33-36}

Although some retrospective studies suggest that oral anticoagulation may be discontinued safely in selected patients after successful ablation, there is no definitive evidence that maintenance of sinus rhythm after ablation decreases the risk of stroke. Given the risk of asymptomatic (silent) recurrent atrial fibrillation, the true recurrence rate is underestimated. As a result, discontinuing oral anticoagulation in patients in whom the CHADS\textsuperscript{2} score is greater than 1 is problematic and requires vigilant and frequent follow-up.
Guideline

In 2007, the expert consensus statement on catheter and surgical ablation of atrial fibrillation by the HRS/EHRA/ECAS concluded that the primary indication for catheter ablation is the presence of symptomatic atrial fibrillation that is refractory or intolerant to at least one class 1 or class 3 antiarrhythmic drug. It also concluded that catheter ablation is appropriate in selected symptomatic patients with heart failure, a reduced ejection fraction, or both. The 2011 update to the guidelines for the treatment of patients with atrial fibrillation by the American College of Cardiology, the American Heart Association, and the HRS states that “catheter ablation performed in experienced centers is useful in maintaining sinus rhythm in selected significantly symptomatic patients who have failed treatment with an antiarrhythmic drug and have normal or mildly dilated left atria, normal or mildly reduced left ventricular function, and no severe pulmonary disease.” The 2011 European Society of Cardiology guidelines also endorse catheter ablation for paroxysmal and persistent atrial fibrillation in symptomatic patients in whom antiarrhythmic therapy has failed.

Recommendation

The patient in the vignette has highly symptomatic atrial fibrillation. His dysrhythmia has pro-

Table 1. Adverse Effects of Ablation for Atrial Fibrillation.*

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Incidence</th>
<th>Recommended Monitoring</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.15</td>
<td></td>
<td>Reversal of anticoagulation, immediate pericardiocentesis, surgery if accumulation is ongoing</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>1.2–6.0</td>
<td>Blood-pressure monitoring, examination of cardiac silhouette on chest radiographic study, echocardiography</td>
<td>Pericardiocentesis, surgery if accumulation is ongoing</td>
</tr>
<tr>
<td>Stroke</td>
<td>0–2</td>
<td>Neurologic examination</td>
<td>Depends on center; consider thrombolysis or intervention</td>
</tr>
<tr>
<td>Pulmonary-vein stenosis</td>
<td>0.5–2.0</td>
<td>CT or MRI 3–4 mo after ablation</td>
<td>If stenosis is severe, with symptoms, then dilation and possible stenting of the pulmonary vein or veins</td>
</tr>
<tr>
<td>Phrenic-nerve injury</td>
<td>0–11</td>
<td>Fluoroscopy</td>
<td>Most patients recover without treatment</td>
</tr>
<tr>
<td>Regular atrial arrhythmia†</td>
<td>5–25</td>
<td>Transtelephonic monitoring, Holter monitoring, use of implantable loop recorder</td>
<td>Antiarrhythmic drugs, perform ablation again</td>
</tr>
<tr>
<td>Vascular complications</td>
<td>0.5–5.0</td>
<td>Vascular ultrasonography</td>
<td>Percutaneous or open vascular surgery</td>
</tr>
<tr>
<td>(arteriovenous fistula, pseudoaneurysm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophageal injury with ulceration</td>
<td>10</td>
<td>Esophageal temperature probe</td>
<td>Most patients heal without treatment</td>
</tr>
<tr>
<td>Atrioesophageal fistula</td>
<td>0.04</td>
<td>Maintain high index of suspicion for this complication (symptoms such as fever, chills, recurrent neurologic events, or sepsis occur 2–4 wk after ablation); CT or MRI</td>
<td>Surgery</td>
</tr>
</tbody>
</table>

* CT denotes computed tomography, and MRI magnetic resonance imaging.
† “Regular atrial arrhythmia” is a term used to describe both atrial tachycardia and an atypical form of atrial flutter after ablation that can occur with incomplete pulmonary-vein isolation.
gressed from paroxysmal to persistent atrial fibrillation despite antiarrhythmic drug therapy. He would be a suitable candidate for pulmonary-vein isolation with either radiofrequency ablation or cryoablation, with a projected success rate of 80 to 85%. If he were allowed to lapse into permanent atrial fibrillation, the success rate would be lower. The physician is obligated to provide the patient with unbiased information and to explain the possible outcomes and complications of ablation. It should be stressed that ablation is performed for symptom relief and to improve the quality of life and that it has not been proved to decrease the risk of stroke or to improve longevity. The patient should be informed that comprehensive arrhythmia monitoring and follow-up will be needed after the ablation and that recurrence of atrial fibrillation is common and may require another trial of antiarrhythmic drugs or a second ablation. It is important to emphasize that even if the ablation is successful, the decision to discontinue oral anticoagulation must be weighed very carefully and discontinuation may be inadvisable. Extended monitoring may be required to make this decision.

No potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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