Catheter Ablation as Treatment for Atrial Fibrillation

I. Description

Radiofrequency ablation (RFA) using a percutaneous catheter-based approach is widely used to treat supraventricular arrhythmias. Atrial fibrillation (AF) frequently arises from an abnormal focus at or near the junction of the pulmonary veins and the left atrium, thus leading to the feasibility of more focused ablation techniques directed at these structures. Catheter-based ablation, using both RFA and cryoablation, is being studied in the treatment of various types of AF.

Results of randomized, controlled trials (RCTs) that compare RFA with antiarrhythmic medications report that freedom from AF is more likely following ablation compared with medications. Results of long-term follow-up of 5 to 6 years following ablation demonstrate that late recurrences continue to occur in patients who are free of AF at 1 year. However, most patients who are AF-free at 1 year remain AF-free at 5 to 6 years. Rates of complications following ablation remain somewhat uncertain. Death is rare, and a 2013 systematic review including more than 83,000 patients reported a major complication rate of 2.9%. The available evidence is sufficient to draw conclusions and to determine that outcomes are improved with use of catheter ablation of arrhythmogenic foci or to electrically isolate the pulmonary veins for symptomatic paroxysmal or persistent AF, when antiarrhythmic medications have failed to adequately control symptoms. Two RCTs have evaluated use of catheter ablation as an initial strategy for paroxysmal AF, with somewhat mixed findings, although both studies demonstrated benefits to catheter ablation on at least some outcomes. Given the RCT results and supportive clinical input, the available evidence is sufficient to draw conclusions and to determine that outcomes are improved for use of catheter ablation as an initial strategy for symptomatic paroxysmal AF.

Nonrandomized studies of cryoablation report success rates in the range seen for RFA, and 1 RCT suggests that cryoablation is more effective than medications. Two additional small RCTs compare cryoablation with RFA but are limited by their short-term follow-up and by the comparison device used. In both of these studies, RFA had an unusually low success rate. Use of transcatheter cryoablation as an alternative to RFA for the treatment of AF is supported by clinical input.
Therefore, the available evidence is sufficient to draw conclusions and to determine that outcomes are improved for use of cryoablation as an alternative RFA.

Repeat procedures are common within the first year after initial ablation and are associated with an incremental improvement in maintenance of sinus rhythm. These repeat procedures are of a more limited nature compared with the initial ablation, targeting specific areas where ablation may not be complete, and/or a focused ablation for treatment of postablation atrial flutter. Given the evidence demonstrating improved outcomes for initial catheter ablations for AF, repeat procedures, generally up to 2 repeat ablations, may therefore be considered to improve outcomes for patients with AF.

Background

AF is the most common cardiac arrhythmia, with a prevalence estimated at 0.4% of the population, increasing with age. The underlying mechanism of AF involves interplay between electrical triggering events and the myocardial substrate that permits propagation and maintenance of the aberrant electrical circuit. The most common focal trigger of AF appears to be located within the cardiac muscle that extends into the pulmonary veins.

AF accounts for approximately one-third of hospitalizations for cardiac rhythm disturbances. Symptoms of AF (e.g., palpitations; decreased exercise tolerance; dyspnea) are primarily related to poorly controlled or irregular heart rate. The loss of atrioventricular (AV) synchrony results in a decreased cardiac output, which can be significant in patients with compromised cardiac function. In addition, patients with AF are at higher risk for stroke, and anticoagulation is typically recommended. AF is also associated with other cardiac conditions, such as valvular heart disease, heart failure, hypertension, and diabetes. Although episodes of AF can be converted to normal sinus rhythm using either pharmacologic or electroshock conversion, the natural history of AF is one of recurrence, thought to be related to fibrillation-induced anatomic and electrical remodeling of the atria.

AF can be subdivided into 3 types:
- paroxysmal (episodes that last fewer than 7 days and are self-terminating),
- persistent (episodes that last for more than 7 days and can be terminated pharmacologically or by electrical cardioversion), or
- permanent

Treatment strategies can be broadly subdivided into rate control, in which only the ventricular rate is controlled and the atria are allowed to fibrillate, or rhythm control, in which there is an attempt to reestablish and maintain normal sinus rhythm. Rhythm control has long been considered an important treatment goal for management of AF, although its primacy has recently been challenged by the results of several randomized trials that reported that pharmacologically maintained rhythm control offered no improvement in mortality or cardiovascular morbidity compared with rate control.
Currently, the main indications for a rhythm control strategy are for patients with paroxysmal or persistent AF who have hemodynamic compromise associated with episodes of AF or who have bothersome symptoms, despite adequate rate control. A rhythm-control strategy involves initial pharmacologic or electronic cardioversion, followed by pharmacologic treatment to maintain normal sinus rhythm. However, antiarrhythmic medications are often not effective in maintaining sinus rhythm. As a result, episodes of recurrent AF are typical, and patients with persistent AF may require multiple episodes of cardioversion. Implantable atrial defibrillators, which are designed to detect and terminate an episode of AF, are an alternative in patients otherwise requiring serial cardioversions, but these have not yet achieved widespread use. Patients with paroxysmal AF, by definition, do not require cardioversion but may be treated pharmacologically to prevent further arrhythmic episodes.

Treatment of permanent AF focuses on rate control, using either pharmacologic therapy or ablation of the AV node, followed by ventricular pacing. Although AV nodal ablation produces symptomatic improvement, it does entail lifelong anticoagulation (due to the ongoing fibrillation of the atria), loss of AV synchrony, and lifelong pacemaker dependency. Implantable defibrillators are contraindicated in patients with permanent AF.

The cited treatment options are not considered curative. A variety of ablative procedures have been investigated as potentially curative approaches, or perhaps modifying the arrhythmia such that drug therapy becomes more effective. Ablative approaches focus on interruption of the electrical pathways that contribute to AF through modifying the arrhythmia triggers and/or the myocardial substrate that maintains the aberrant rhythm. The Maze procedure, an open surgical procedure often combined with other cardiac surgeries (e.g., valve repair), is an ablative procedure that involves sequential atriotomy incisions designed to create electrical barriers that prevent the maintenance of AF. Because of the highly invasive nature of this procedure, it is currently mainly reserved for patients who are undergoing open heart surgery for other reasons, such as valve repair or coronary artery bypass grafting.

RFA using a percutaneous catheter-based approach is a widely used technique for a variety of supraventricular arrhythmias, in which intracardiac mapping identifies a discrete arrhythmogenic focus that is the target of ablation. The situation is more complex for AF because there is not a single arrhythmogenic focus. Since the inception of ablation techniques in the early 1990s, there has been a progressive understanding of the underlying electrical pathways in the heart that are associated with AF. In the late 1990s, it was recognized that AF most frequently arose from an abnormal focus at or near the junction of the pulmonary veins and the left atrium, thus leading to the feasibility of more focused, percutaneous ablation techniques. The basic strategies that have emerged for focal ablation within the pulmonary veins, as identified by electrophysiologic mapping, are segmental ostial ablation guided by pulmonary vein potential (electrical approach), or circumferential pulmonary vein ablation (anatomic approach). Circumferential pulmonary vein ablation using radiofrequency energy is the most commonly used approach at the present time. The procedure also can be done using cryoablation technology. Use of currently available catheters for AF has a steep learning curve because they require extensive guiding to multiple ablation points. One of the potential advantages to cryoablation techniques is that cryoablation catheters...
have a circular or shaped end point, allowing a “one-shot” ablation. Other types of radiofrequency catheters, such as Medtronic’s radiofrequency-based Pulmonary Vein Ablation Catheter®, that incorporate circular or otherwise shaped end points are under investigation.

Repeat procedures following an initial RFA are commonly performed if AF recurs or if atrial flutter develops postprocedure. The need for repeat procedures may, in part, depend on clinical characteristics of the patient (e.g., age, persistent vs. paroxysmal AF, atrial dilatation), and the type of initial ablation performed. Repeat procedures are generally more limited than the initial procedure. For example, in cases where electrical reconnections occur as a result of incomplete ablation lines, a “touch up” procedure is done to correct gaps in the original ablation. In other cases where atrial flutter develops following ablation, a “flutter ablation” is performed, which is more limited than the original AF ablation procedure. A number of clinical and demographic factors have been associated with the need for a second procedure, including age, length of AF, permanent AF, left atrial size, and left ventricular ejection fraction.

Regulatory Status
In February 2009, the NaviStar® ThermoCool® Irrigated Deflectable Diagnostic/Ablation Catheter and EZ Steer ThermoCool NAV Catheter (Biosense Webster) were approved by the U.S. Food and Drug Administration (FDA) through the premarket approval (PMA) process for “catheter-based cardiac electrophysiological mapping (stimulating and recording), and when used with the Stockert 70 generator, for the treatment of a) type I atrial flutter in patients age 18 or older; b) recurrent drug/device refractory sustained monomorphic ventricular tachycardia (VT) due to prior myocardial infarction (MI) in adults; c) drug refractory recurrent symptomatic paroxysmal AF, when used with compatible 3-dimensional electroanatomic mapping systems” (for RFA).

In December 2010, Medtronic’s Arctic Front® Cardiac CryoAblation Catheter and CryoConsole were approved by FDA for the “treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation.” In addition, Medtronic’s Freezor® MAX Cardiac CryoAblation Catheter was approved as an adjunctive device to be used in conjunction with the Arctic Front system for “gap cryoablation to complete electrical isolation of the pulmonary veins, cryoablation of focal trigger sites, and creation of ablation line between the inferior vena cava and the tricuspid valve” (for cryoablation).

In addition, FDA has also granted PMA approval to numerous catheter ablation systems for other ablation therapy for arrhythmias such as supraventricular tachycardia, atrial flutter, and VT.

II. Criteria/Guidelines
A. Transcatheter radiofrequency ablation or cryoablation to treat atrial fibrillation is covered (subject to Limitations and Administrative Guidelines) as a treatment for either of the following indications which have failed to respond to adequate trials of antiarrhythmic medications:
   1. Symptomatic paroxysmal or symptomatic persistent atrial fibrillation; or
   2. As an alternative to atioventricular nodal ablation and pacemaker insertion in patients with class II or III congestive heart failure and symptomatic atrial fibrillation.
B. Transcatheter radiofrequency ablation or cryoablation to treat atrial fibrillation is covered (subject to Limitations and Administrative Guidelines) as an initial treatment for patients with symptomatic paroxysmal atrial fibrillation in whom a rhythm-control strategy is desired.
C. Repeat radiofrequency ablation or cryoablation is covered (subject to Limitations and Administrative Guidelines) in patients with recurrence of atrial fibrillation and/or development of atrial flutter following the initial procedure.

III. Limitations

Transcatheter ablation to treat atrial fibrillation as a treatment for cases of atrial fibrillation that do not meet the criteria outlined above is not covered as it is not known to improve health outcomes.

IV. Administrative Guidelines

A. Precertification is not required. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria.
B. Transcatheter treatment of atrial fibrillation may include pulmonary vein isolation and/or focal ablation.
C. Beginning in 2013, there is a new CPT code specific to pulmonary vein ablation: 93656: Comprehensive electrophysiologic evaluation including transseptal catheterizations, insertion and repositioning of multiple electrode catheters with induction or attempted induction of an arrhythmia with atrial recording and pacing, when possible, right ventricular pacing and recording, His bundle recording with intracardiac catheter ablation of arrhythmogenic focus, with treatment of atrial fibrillation by ablation by pulmonary vein isolation.

This new combination code is not to be used with any of the following CPT codes: 93279-93284, 93286-93289, 93462, 93600, 93602, 93603, 93610, 93612, 93618, 93619, 93620, 93621, 93653, or 93654.

There is also a CPT add-on code for additional atrial fibrillation therapy after the pulmonary vein isolation procedure:

93657: Additional linear or focal intracardiac catheter ablation of the left or right atrium for treatment of atrial fibrillation remaining after completion of pulmonary vein isolation (List separately in addition to code for primary procedure)

There is not one single procedure for catheter ablation, but several variations. Electrical isolation of the pulmonary vein musculature (pulmonary vein isolation) is the cornerstone of most AF ablation procedures, but additional ablation sites may also be included during the initial ablation. Potential additional ablation procedures include: creation of linear lesions within the left atrium; ablation of focal triggers outside the pulmonary veins; ablation of areas with complex fractionated atrial electrograms; and ablation of left atrial ganglionated plexi. The specific ablation sites may be determined by electroanatomic mapping to identify additional
sites of excitation. As a result, sites may vary from patient to patient, even if they are treated by the same physician. Patients with long-standing persistent AF may need more extensive ablation. Similarly, repeat ablation procedures for recurrent AF generally involve more extensive ablation than do initial procedures.

As many as 30% of patients will require a follow-up (repeat) procedure due to recurrence of AF or to developing atrial flutter. In most of the published studies, success rates were based on having as many as 3 separate procedures, although these repeat procedures may be more limited than the initial procedure.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>93656</td>
<td>Comprehensive electrophysiologic evaluation including transseptal catheterizations, insertion and repositioning of multiple electrode catheters with induction or attempted induction of an arrhythmia with atrial recording and pacing, when possible, right ventricular pacing and recording, His bundle recording with intracardiac catheter ablation of arrhythmogenic focus, with treatment of atrial fibrillation by ablation by pulmonary vein isolation</td>
</tr>
<tr>
<td>93657</td>
<td>Additional linear or focal intracardiac catheter ablation of the left or right atrium for treatment of atrial fibrillation remaining after completion of pulmonary vein isolation (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>93799</td>
<td>Unlisted cardiovascular service or procedure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-9 Diagnosis</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>427.31</td>
<td>Atrial fibrillation and flutter</td>
</tr>
<tr>
<td>428.0</td>
<td>Congestive heart failure, unspecified</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-9 Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>37.34</td>
<td>Excision or destruction of other lesion or tissue of heart, other approach (i.e., ablation of heart tissue via peripherally inserted catheter)</td>
</tr>
</tbody>
</table>

ICD-10 codes are provided for your information. These will not become effective until 10/01/2015.

<table>
<thead>
<tr>
<th>ICD-10-PCS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>02SS42ZZ, 02ST42ZZ</td>
<td>Destruction, heart and great vessels, pulmonary veins, percutaneous endoscopic, code list</td>
</tr>
</tbody>
</table>
V. Scientific Background

This policy was originally created in 2004 and updated periodically with literature review since that time. The most recent literature search was performed through February 3, 2015. Following is a summary of the key literature to date.

In patients with paroxysmal or persistent atrial fibrillation (AF), catheter ablation may be considered an alternative to drug therapy. In patients with permanent AF, catheter ablation may be considered an alternative to drug therapy or to atroventricular (AV) nodal ablation and pacing. For all types of AF, it is possible that catheter ablation may not be curative as a sole treatment but might alter the underlying myocardial triggers or substrate in such a way that subsequent pharmacologic therapy may become more effective.

There is ongoing controversy regarding the relative benefits of rhythm versus rate control in AF, which underlies the evaluation of evidence on catheter ablation. Randomized trials of pharmacologic therapies have not demonstrated the superiority of rhythm versus rate control. However, the apparent equivalency of these 2 strategies with pharmacologic therapy cannot be extrapolated to the rhythm control achieved with ablation. Antiarrhythmic medications used for rhythm control are only partially effective and have serious complications, including proarrhythmic properties, which can be lethal. Therefore, nonpharmacologic strategies for rhythm control have the potential to achieve superior outcomes than have been seen with pharmacologic strategies.

Outcome Assessment in AF

A variety of outcomes for treatment of AF may be considered. The mortality and morbidity related to AF, such as cardiovascular mortality, stroke, and heart failure, are the most important clinical outcomes. However, these are uncommon events, and currently available trials are not powered to detect differences in these outcomes. Quality of life (QOL) is also an important outcome, as these measures reflect important manifestations of AF, such as symptoms and reduced exercise tolerance. AF has been shown to be associated with lower QOL scores, and maintenance of sinus rhythm has been associated with higher QOL scores for patients with paroxysmal AF.

Recurrence of AF is a more problematic outcome measure, because the intermittent and often transient nature of recurrences makes accurate measurement difficult. This outcome measure has been reported in different ways. For example, the proportion of patients in sinus rhythm at the end of the study, the time to first recurrence, and the number of recurrences within a time period have been reported. A recent publication highlights the difficulties in measuring AF recurrence and recommends a measure of AF “burden,” defined as the percentage of time an individual is in AF, as the optimal measure of treatment efficacy. However, this parameter requires continuous monitoring over a relatively long period of time, which is inconvenient for patients, resource intensive, and usually not pragmatic in patients who do not already have an implanted pacemaker.

Recommendations for outcome assessment in trials of AF treatment were included in the 2006 American College of Cardiology/American Heart Association practice guidelines for the treatment of AF. These guidelines pointed out that the appropriate end points for evaluation of treatment
efficacy in patients with paroxysmal or persistent AF have little in common. For example, in studies of persistent AF, the proportion of patients in sinus rhythm at the end of follow-up is a useful end point, but this is a less useful measure in studies of paroxysmal AF. Given all these variables, ideally, controlled clinical trials would report a range of outcomes (including QOL) and complications in homogeneous patient groups and compare with the most relevant treatment alternatives, such as pharmacologic therapy; defibrillator therapy; and AV nodal ablation, depending on the classification of AF (paroxysmal, persistent, permanent).

Radiofrequency Ablation for AF

Systematic Reviews

The literature review for this policy was originally based on a 2008 TEC Assessment. Six randomized controlled trials (RCTs) met the inclusion criteria for this TEC Assessment. The trials differed in their patient populations, the specific catheter ablation techniques used, and the comparisons made. The trials addressed 3 distinct indications for catheter ablation: (1) patients with paroxysmal AF, as a first-line treatment option (n=1 trial); (2) patients with symptomatic paroxysmal or persistent AF who have failed treatment with antiarrhythmic drugs (n=4 trials); and (3) patients with symptomatic AF and heart failure who have failed treatment with standard medications for rate control and who would otherwise be considered for AV nodal ablation and pacemaker insertion (n=1 trial).

All 6 trials reported that maintenance of sinus rhythm was improved for the catheter ablation group. Recurrence rates of AF at 1 year ranged from 11 to 44% for the catheter ablation groups in these trials, compared with 63 to 96% for the medication groups. Four of the 6 trials reported QOL outcomes. One of these only reported within-group comparisons, as opposed to between-group comparisons. The other 3 trials reported improvements in QOL associated with catheter ablation. These QOL measures were self-reported, and because both trials were unblinded, there is the possibility of reporting bias due to placebo effect.

None of the available trials reported meaningful data on cardiovascular morbidity and mortality associated with AF. The Assessment concluded that radiofrequency catheter ablation is more effective than medications in maintaining sinus rhythm across a wide spectrum of patients with AF and across different variations of catheter ablation. The evidence on QOL is suggestive, but not definitive, of a benefit for patients undergoing catheter ablation. For other outcomes, the evidence did not permit conclusions. It was not possible to estimate the rate of serious complications, such as pulmonary vein stenosis, cardiac tamponade, or atrioesophageal fistula with precision given the limited number of patients in the trials and the continued evolution of the technique. However, the rate of serious complications is expected to be low, likely in the 1 to 5% range.

Based on these findings, TEC criteria were met for 2 indications: patients with symptomatic paroxysmal or persistent AF who have failed treatment with antiarrhythmic drugs and patients with symptomatic AF and heart failure who have failed treatment with standard medications for rate control and who would otherwise be considered for AV nodal ablation and pacemaker insertion. For the first indication, the conclusion followed from the premise that reducing episodes of
Catheter Ablation as Treatment for Atrial Fibrillation

recurrent AF for this population will reduce or eliminate the symptoms associated with episodes of AF. For the other indication, the single multicenter RCT available was judged sufficient to conclude that catheter ablation improved outcomes compared with the alternative, AV nodal ablation and pacemaker insertion. While this trial was relatively small, it was judged to be otherwise of high quality and reported improvements of a relatively large magnitude across a range of clinically important outcome measures, including QOL, exercise tolerance, left-ventricular ejection fraction (LVEF), and maintenance of sinus rhythm.

Since the publication of the 2008 TEC Assessment, several additional systematic reviews and meta-analyses of catheter ablation for AF have been published. A Cochrane Review on catheter ablation for paroxysmal and persistent AF was published in 2012. This review included 7 RCTs of catheter ablation versus medical therapy. Main conclusions were that catheter ablation was superior at reducing the recurrence of AF (risk ratio [RR], 0.27; 95% confidence interval [CI], 0.18 to 0.41) but that there were no differences in mortality (RR=0.50; 95% CI, 0.04 to 5.65), embolic complications (RR=1.01; 95% CI, 0.18 to 5.68), or death from thromboembolism (RR=3.04; 95% CI, 0.13 to 73.4).

In 2013, Ganesan and colleagues published results from a systematic review and meta-analysis of studies reporting long-term outcomes after percutaneous catheter ablation for paroxysmal and nonparoxysmal AF. The authors included 19 studies (RCTs, case-control and cohort studies, case series) that reported catheter ablation outcomes at 3 years or more after the index ablation procedures. Sample sizes in these studies ranged from 39 to 1404, with a total of 6167 patients included overall. For a single procedure, the pooled overall success rate at 12 months postprocedure was 64.2% (95% CI, 57.5% to 70.3%). At late follow-up, the overall single-procedure success, defined as freedom from atrial arrhythmia at latest follow-up, was 53.1% (95% CI, 46.2% to 60.0%). The pooled overall multiple-procedure long-term success rate was 79.8% (95% CI, 75.0% to 83.8%). The analysis was unable to identify any predictors of short- or long-term recurrence. Reporting of periprocedural complications was heterogeneous across the studies, but complication rates were generally low.

Three systematic reviews and meta-analyses comparing RFA with antiarrhythmic drug therapy for AF were published from 2008 to 2009. Nair and colleagues included 6 RCTs comparing RFA with antiarrhythmic drug therapy for AF, five of which were included in the TEC Assessment. Two systematic reviews published in 2008 summarized and synthesized the RCT evidence on catheter ablation versus alternate therapy. These reviews included 4 of the 6 trials reviewed for the TEC Assessment. Noheria and colleagues included 3 of these 4 RCTs, as well as an additional small RCT of 30 patients not included in the TEC Assessment. Gjesdal and colleagues included 5 RCTs in their analysis, including the 4 trials in the Noheria and colleagues systematic review, and 1 additional trial (included in the TEC Assessment) that compared catheter ablation plus antiarrhythmic drugs with antiarrhythmic drugs alone. All 3 systematic reviews concluded that catheter ablation was more effective than pharmacologic treatment in maintaining normal sinus rhythm. Nair and colleagues demonstrated a pooled relative risk for AF at 1 year after procedure of 0.35 compared with antiarrhythmic drug therapy. In combined analysis, Noheria and colleagues reported AF-free survival at 1 year to be 75.7% in the catheter ablation group compared with 18.8% in the comparison group. The relative risk for maintaining sinus rhythm was 3.73 (95% CI, 2.47 to 5.63) for
the catheter-ablation group compared with alternative treatment. Gjesdal and colleagues concluded that the available evidence was of moderate quality and consistent in reporting that AF-free survival was superior for the catheter ablation group. However, due to unexplained heterogeneity, these authors did not perform a combined analysis.

More recent systematic reviews have assessed the effect of radiofrequency ablation (RFA) on a variety of AF-related outcomes. In 2014, Zhuang and colleagues conducted a systematic review to evaluate the effect of RFA on left atrial (LA) volume and function in patients with AF. In a summary of data from 26 studies enrolling 1821 patients, RFA was associated in improvements in LA volume measurements compared with preablation (e.g., for LA diameter), the weighted mean difference was -1.52 mm (95% CI -2.57 to -0.47). There were no significant improvements in LA function.

**Randomized Controlled Trials**

Since the TEC Assessment, 7 additional RCTs comparing RFA versus pharmacologic treatment have been identified. Wilber and colleagues enrolled 167 patients who had failed at least 1 antiarrhythmic medication and had at least 3 AF episodes in the prior 6 months. Patients were randomly assigned to either catheter ablation or continued drug therapy and followed for 9 months. At the end of follow-up, 66% of patients in the ablation group were free of recurrent AF compared with 16% of patients in the medication group. Adverse events related to treatment occurred in 4.9% (5/103) of patients treated with ablation and in 8.8% (5/57) of patients treated with medications.

Forleo and colleagues randomly assigned 70 patients with type 2 diabetes and AF to either RFA or an antiarrhythmic medication. Follow-up was for 1 year, with the primary outcome being recurrence of AF. At the end of the trial, 42.9% of patients in the medication group were free of AF compared with 80% of patients in the ablation group. There was also a significant improvement in QOL for patients in the ablation group. Adverse events from medications occurred in 17.2% (6/35) patients, whereas complications from ablation occurred in 2.9% (1/35).

Mont and colleagues conducted an RCT comparing radiofrequency catheter ablation with antiarrhythmic drug therapy among 146 patients with symptomatic persistent AF. Patients were randomized in a 2:1 fashion to catheter ablation (n=98) or antiarrhythmic drug therapy (N=48). Although the study was terminated before the planned sample size of 208 was met due to lower than expected enrollment, at 12 months of follow-up, the proportion of patients who were free of sustained episodes of AF was higher in the catheter ablation group than the antiarrhythmic drug therapy group (70.4% vs 43.7%, p=0.002). QOL scores did not significantly differ between the groups. Longer term outcomes were not reported.

**RFA as First-Line Therapy for AF**

Several studies have evaluated RFA ablation as first-line therapy for AF. In 2014, Morillo and colleagues published results of the RAAFT-2 trial, an RCT to compare RFA with antiarrhythmic drug therapy as first-line therapy for paroxysmal AF. Eligible patients had symptomatic recurrent paroxysmal AF lasting more than 30 seconds, with 4 or fewer episodes in the prior 6 months, and
had no previous antiarrhythmic drug treatment. The study enrolled 127 patients at 16 centers; 66 were randomized to RFA and 61 to antiarrhythmic drug therapy, at the discretion of the treating physician. In the ablation group, 63 underwent ablation; during follow up, 9 underwent reablation and 6 crossed over to receive antiarrhythmic drug therapy. In the drug therapy group, 26 crossed over to undergo ablation and 24 discontinued antiarrhythmic drug therapy. Analysis was intention-to-treat. Patients were followed with biweekly scheduled transtelemphonic monitor recordings and symptomatic recordings through the 24-month follow-up period. The study’s primary outcome, recurrence of any atrial tachyarrhythmia lasting longer than 30 seconds, occurred in 72.1% (n=44) in the antiarrhythmic drug group, compared with 54.5% (n=36) in the ablation group (hazard ratio [HR], 0.56; 95% CI, 0.35 to 0.90; p=0.02). Fewer patients in the RFA group had recurrence of symptomatic AF, atrial flutter, or atrial tachycardia (47% vs 59%; HR=0.56, 95% CI, 0.33 to 0.95; p=0.03) or recurrence of symptomatic AF (415 vs 57%; HR=0.52, 95% CI, 0.3 to 0.89; p=0.02). QOL measures did not differ significantly between groups.

An earlier RCT of RFA ablation as the initial therapy for paroxysmal AF was published in 2012. A total of 294 patients were randomized to initial treatment with catheter ablation or pharmacologic therapy. Patients were followed for up to 24 months for the primary outcomes of burden of AF (percent of time in AF on Holter monitor) at each time point and cumulative burden of AF over all time points. For the individual time points, the burden of AF was lower in the catheter ablation group at 24 months (9% versus 18%, p=0.007), but not at other time points. The cumulative burden did not differ significantly for the catheter ablation group compared with pharmacologic therapy (90th percentile of cumulative burden, 13% vs 19%, p=0.10). The secondary outcome of percent of patients free from AF at 24 months was greater for the catheter ablation group (85% vs 71%, p=0.004), as was the secondary outcome of freedom from symptomatic AF (93% vs 84%, p=0.01). There was 1 death in the ablation group due to a procedural-related stroke, and 3 patients in the ablation group developed cardiac tamponade following the procedure.

Results of an RCT comparing ablation with amiodarone for persistent AF in 203 patients with heart failure have been presented in abstract form. Preliminary results demonstrate lower rates of AF recurrence in patients treated with RFA (HR for AF recurrence in amiodarone group compared with RFA group, 2.5; 95% CI, 1.5 to 4.3; p<0.001).

**RFA for AF in the Setting of Heart Failure**

Several studies have compared catheter ablation with medical therapy for AF in the setting of heart failure. Hunter and colleagues conducted an RCT comparing catheter ablation with medical rate control for patients with persistent AF and symptomatic heart failure, with adequate rate control at the time of enrollment. There was no requirement for patients to have failed antiarrhythmic drug therapy. The study’s primary end point was difference between groups in LVEF at 6 months postprocedure. Fifty patients were randomized, 26 to catheter ablation and 24 to medical management. At 6 months, 81% of the catheter ablation group was free from recurrent AF off antiarrhythmic drugs. LVEF at 6 months after procedure was 40% (±12%) in the catheter ablation group, compared with 31% (±13%, p=0.015). Catheter ablation was also associated with improvements in health-related QOL. Jones and colleagues reported results from an RCT comparing
catheter ablation with medical rate control for patients with symptomatic heart failure, LVEF 35% or less, and persistent AF. Fifty-two patients were randomized, 26 each to catheter ablation or medical rate control. At 12 months after procedure, sinus rhythm was maintained in 88% of the catheter ablation group, with a single-procedure success rate of 68%. For the study’s primary outcome, peak oxygen consumption at 12 months after procedure, there was a significant increase in the catheter ablation group compared with the medical management group (+3.07 mL/kg/min; 95% CI, 0.56 to 5.59; p=0.018).

**Longer-Term Outcomes**

The available RCTs mainly report on short-term outcomes up to 1 year and, therefore, do not evaluate the rate of late recurrences after 1 year. Longer term outcomes have been reported by several authors. These studies generally report rates of early recurrence in the range of 20 to 30%, requiring repeat ablations. Rates of longer term recurrence are lower if early recurrence does not occur, in the range of 1 to 2% per year.

Hussein and colleagues reported on 831 patients who were treated in 2005, with a median follow-up of 55 months. During the first year following ablation, 23.8% had a recurrence of AF. During the remaining follow-up, recurrences occurred in 8.9% additional patients. The overall rate of arrhythmia-free and off drugs was 79.4% at 55 months. An additional 10.5% of patients were arrhythmia-free on drugs, for a total rate of 89.9% clinical improvement.

In 2013, Bunch and colleagues reported results from a prospective cohort study comparing risk of stroke between patients with AF who had undergone catheter ablation, patients with AF who did not undergo ablation, and patients without a history of AF. A total of 4212 patients with AF who had undergone catheter ablation were age- and sex-matched in a 1:4 ratio to 16,848 subjects in each of the other groups. The mean follow up time was 3.9 years. At 1 year postprocedure, significantly more patients with AF who did not undergo ablation had a stroke (3.5%) than those with AF who underwent ablation (1.4%) or had no history of AF (1.4%; p<0.001 for trend). During the follow-up period, for all ages and CHADS2 profiles, patients with AF who had ablation had a lower stroke risk than those with AF without ablation.

Several smaller studies have also reported longer term follow-up after radiofrequency catheter ablation. Weerasooriya and colleagues reported 5-year follow-up in 100 patients treated with catheter ablation. Recurrences were most common within the first 6 months, with repeat procedures being common during that period. At 1, 2, and 5 years after ablation, arrhythmia-free survival was 87%, 81%, and 63%, respectively. Tzou and colleagues reported long-term follow-up for 123 patients who had a previous successful ablation, defined as free of AF at 1 year. At 3 years of follow-up, 85% of patients were still free of AF and off of all medications, and at 5 years, 71% remained free of AF. The authors estimated a late recurrence rate of approximately 7% per year for patients with an initial successful procedure. In a similar study, Bertaglia and colleagues reported outcomes after 6 years of follow-up for 229 patients who had a single, successful ablation. At 1-year follow-up, 77% of patients (177/229) were free of AF and off of all medications. After a mean additional follow-up of 49.7 ± 13.3 months for these 177 patients, 58% remained free of AF. Sawhney and colleagues reported 5-year success rates in 71 patients who underwent ablation in
2002 or 2003. Freedom from symptomatic AF off medications was achieved in 86% of patients at 1 year, 79% at 2 years, and 56% at 5 years. A substantial minority of patients (22.5%) had recurrence at times greater than 2 years after ablation. A 2013 study by Anselmino and colleagues followed 196 patients who underwent radiofrequency catheter ablation for paroxysmal or persistent AF and had LVEF 50% or less for a mean of 46.2 months. During follow-up, 29.6% of patients required repeat ablation procedures. At the end of follow up, 37.8% had at least 1 episode of AF, atrial flutter, or ectopic atrial tachycardia. Takigawa and colleagues reported long-term follow up for 1220 patients who underwent RFA for symptomatic paroxysmal AF. AF recurrence-free survival probabilities at 5 years were 59.4% after the initial procedure and 81.1% after the final ablation procedure, with an average of 1.3 procedures per patient.

**Section Summary**

Numerous RCTs of RFA for isolation of the pulmonary veins versus medical management report that freedom from AF at 1 year is higher with RFA compared to medical management. The trials mainly include patients who have failed antiarrhythmic medications, although 2 trials treat patients with paroxysmal AF as initial treatment. These studies report that most patients undergoing RFA are free of AF at 1 year. QOL is also improved in these trials for patients undergoing catheter ablation. A smaller number of studies evaluate outcomes longer than 1 year and report that late recurrences occur up to 5 years but are uncommon after the first year. Complications from RFA are reported at low rates in the RCTs, but the numbers of patients in these trials are too low to accurately estimate rates of uncommon events. There is a lack of data on clinical outcomes other than freedom from AF. Larger RCTs are underway to evaluate long-term clinical outcomes such as stroke and mortality. Two RCTs have evaluated the use of catheter ablation as an initial strategy for paroxysmal AF, with somewhat mixed findings, although both studies demonstrated benefits to catheter ablation on at least some outcomes.

**Cryoablation of the Pulmonary Veins**

A number of studies reported outcomes of ablation using cryoablation. Earlier studies were mainly case series and cohort studies reporting success rates in the range of that reported for RFA. Since 2013, several RCTs have been published comparing cryoablation with medical therapy for RFA.

**Randomized Clinical Trials**

In 2013, Packer and colleagues reported results of the STOP-AF trial, an RCT of cryoablation versus antiarrhythmic medications. This study enrolled 245 patients with paroxysmal AF who had failed at least 1 (median, 1.2) membrane-active antiarrhythmic medications. Patients were randomized in 2:1 fashion to either cryoballoon ablation (n=163) or drug therapy (n=82). At 1-year follow-up, 69.9% of patients in the ablation group were free of AF versus 7.3% in the medication group. The single-procedure success rate was 57.7%. There was also a significantly greater reduction in symptoms for the ablation group. Seventy-nine percent of the drug treatment group crossed over to cryoablation during 12 months of study follow-up because of recurrent, persistent AF. Cryoablation procedure-related adverse events occurred in 5 patients (3.1%); major AF events occurred in 3.1% of the cryoablation group compared with 8.5% of the drug-treatment group.
Catheter Ablation as Treatment for Atrial Fibrillation

(Noninferiority p<0.001). Phrenic nerve injury occurred at a rate of 13.5%, with 86% resolved at 12 months.

In 2014, Andrade and colleagues published a follow-up analysis of the STOP-AF trial results to evaluate the incidence and significance of early recurrence of AF after ablation. Of the 163 subjects randomized to cryoablation, 84 patients (51.5%) experienced early recurrence of AF, defined as any recurrence of AF lasting more than 30 seconds between three and 12 months postablation. The presence of early AF recurrence was associated with late AF recurrence: late AF recurrence occurred in 41 patients (25.1%), and was more likely in those with early recurrence (55.6% in those with early recurrence vs 12.7% in those without early recurrence; p<0.001).

The Mesh Ablator versus Cryoballoon Pulmonary Vein Ablation of Symptomatic Paroxysmal AF (MACPAF) study was a single-center RCT comparing cryoablation with RFA with the HD Mesh Ablator Catheter (Bard®, purchased by Boston Scientific in 2013) for AF. The HD Mesh Ablator Catheter, which is not cleared for use in the United States, is a multielectrode RF catheter that involves a mesh electrode that is designed to deliver RF energy to multiple points of contact. Primary short-term results for MACPAF were reported by Koch and colleagues in 2013. The study randomized symptomatic paroxysmal AF to catheter ablation with the Arctic Front® cryoablation catheter or the HD Mesh Ablator. The study’s primary end point was complete isolation of the pulmonary veins at the end of the procedure. Enrollment was initially planned for 108 with symptomatic paroxysmal AF that was inadequately controlled with antiarrhythmic drug treatment. However, at interim analysis, the HD Mesh Ablator demonstrated a lack of efficacy for the primary end point, and the study’s data safety monitoring board prematurely terminated the subject. Forty-four patients with drug-resistant paroxysmal AF were randomized at the time the study was terminated and comprise the intention-to-treat analysis cohort. The per-protocol analysis cohort included 32 patients. Three patients withdrew before the catheter procedure; 9 additional patients were excluded from analysis due to use of a study noncompliant catheter (n=2), identification of a trigger arrhythmia, which was subsequently ablated (n=1), failure of transseptal puncture (n=1), or ablation occurring after the interim analysis (n=5). For the primary end point, by intention-to-treat analysis, complete pulmonary vein isolation was achieved in 13/23 (56.5%) of patients in the cryoablation group, compared with 2/21 (9.5%) of patients in the mesh ablator group (p=0.001). In the per-protocol cryoablation group, 76.5% of subjects had complete pulmonary vein isolation. Major complications included 1 case of retroperitoneal hematoma in the cryoablation group and 1 case of pericardial tamponade requiring drainage in the mesh ablator group.

Malmborg and colleagues reported results from an RCT comparing cryoablation with the Arctic Front® cryoballoon catheter to RFA with the Pulmonary Vein Ablation Catheter®. One hundred ten patients with paroxysmal or persistent AF were randomized, 54 to the cryoablation group and 56 to the RFA group. Complete pulmonary vein isolation was achieved in 98% of the cryoablation group, compared with 93% of the RFA group (p=0.37). At 6-month follow-up, freedom from AF (absence of symptoms and no AF episodes on 7-day Holter monitoring or 12-lead electrocardiogram) without antiarrhythmic drug treatment was achieved in 52% of the cryoablation group and 38% of the RFA group (p=0.13).
Results of the Cryo vs RFA trial (A Randomised Study Comparing Pulmonary Vein Isolation Using the Occluding Cryoballoon, Conventional Radiofrequency Energy, or Both in the Treatment of Atrial Fibrillation; NCT01038115), which was an RCT comparing cryoablation with RFA or a hybrid approach among 237 patients with paroxysmal AF, have been presented in abstract form. Single-procedure success rates at 1 year were higher for cryoablation than for RFA (67% vs 47%; P=0.015). There are ongoing trials of cryoablation versus RFA for AF. The FreezeAF trial (PV-Isolation With the Cryoballoon Versus RF: a Randomized Controlled Prospective Non-inferiority Trial) is a noninferiority RCT comparing cryoablation with RFA for patients with paroxysmal AF. Enrollment of 244 patients is planned, and patients will be followed for at least 1 year. The primary outcome is freedom from AF off all drugs. Secondary outcomes include longer-term success rates, procedural data, and cost-effectiveness. The Fire and Ice trial is another ongoing RCT comparing cryoablation with RFA for patients with symptomatic paroxysmal AF.

Systematic Reviews

A meta-analysis of studies of cryoablation was published in 2011. This analysis included the STOP-AF results in abstract form and a total of 22 other nonrandomized studies, primarily case series. Procedural success was reported in over 98% of cases. At 1 year, the rates of success, as defined by no recurrent AF, were 73% (95% CI, 69% to 77%) for paroxysmal AF and 60% (95% CI, 54% to 66%) for persistent AF. Complications were inconsistently reported among the available studies. The most common complication reported was phrenic nerve palsy, which occurred in 6.4% of patients. Other rates of reported complications were pericardial effusion or tamponade (1.5%), groin complications at insertion site (1.8%), stroke (0.3%), and pulmonic stenosis (0.9%).

Nonrandomized Studies

Case series of cryoablation published prior to the publication of RCTs reported success rates in the range of that reported for RFA. One small matched analysis compared 20 patients undergoing cryoablation with 20 patients undergoing RFA, matched for age, gender, LVEF, and AF history. Freedom from AF at 6 months was 55% for the cryoablation group, compared with 45% for the RFA group, a difference that was not significantly different.

In a large, more recent noncomparative study, Schmidt and colleagues used data from a prospective German registry of catheter ablation procedures to compare RF with cryoablation for paroxysmal AF. The cohort included 905 patients who underwent cryoablation and 2870 patients who underwent RFA who were enrolled from January 2007 to August 2011. The 2 groups were generally similar, with the exception that patients who underwent RFA were significantly more likely to have valve disease (8.1% vs 3.0%, p<0.001) and an ejection fraction 40% or less (2.4% vs 1.2%, p<0.05). Rates of acute success were similar for the 2 groups (97.5% for cryoablation vs 97.6% for RFA, p=0.92), as were rates of major procedure-related adverse cardiac and cerebrovascular events (0.4% for cryoablation vs 0.2% for RFA, p=0.15). The overall procedural complication rates were similar for the 2 groups (4.6% for each group, p=1.0); the rate of postprocedural phrenic nerve palsy was significantly higher for the cryoablation group (2.1% for cryoablation vs 0% for RFA, p=0.15). Long-term follow rates are not reported.
Several studies have also reported on methods to reduce the risk of phrenic nerve injury with cryoballoon ablation, including fluoroscopy of spontaneous breathing and recordings of diaphragmatic electromyograms.

**Longer Term Follow-Up**

Similar to RFA, the available RCTs for cryoablation report primarily on short-term outcomes. Longer term outcomes after cryoablation have been reported by several authors.

Vogt and colleagues reported longer-term follow up for 605 patients who underwent cryoablation for symptomatic, paroxysmal or persistent AF. Follow-up data beyond 12 months were available for 451 patients (median follow-up, 30 months). Of those with follow up available, 278 (61.6%) were free of AF recurrence with no need for repeat procedures after a 3-month blanking period. After 1, 2, and 3 repeat procedures, rates of freedom from AF were 74.9%, 76.2%, and 76.9%, respectively. Phrenic nerve palsy was the most common adverse event, occurring in 2% of patients, all of which resolved within 3 to 9 months. There were 2 periprocedural strokes, and 1 case each of periprocedural pericardial tamponade and pericardial effusion.

Neumann and colleagues reported 5-year outcomes after a single cryoablation procedure among 163 patients with symptomatic, drug-refractory paroxysmal AF. Fifty-three percent of subjects were free from recurrent AF, atrial tachycardia, or atrial flutter at 5 years of follow-up with no additional procedures (after a 3-month blanking period).

**Section Summary**

The evidence related to cryoablation for AF includes 3 RCTs and numerous uncontrolled case series. The STOP AF trial, which compared cryoablation with antiarrhythmic medication therapy, reported that cryoablation is superior to medical management, and that rates of freedom from arrhythmia at 1 year in the cryoablation group are in the range reported with RFA. Nonrandomized studies also report that cryoablation has efficacy in the same range as RFA. However, data from randomized trials directly comparing cryoablation with RFA are limited. Interpretation of the MACPAF study is limited by early termination due to unexpectedly low efficacy of the RFA method used. While the Malmborg and colleagues study is suggestive that cryoablation is comparable with RFA, success in the RFA group was also unusually low. This study is also limited by relatively short-term follow-up (6 months) and use of a catheter that is not cleared for use in the United States.

Several ongoing RCTs, particularly the FreezeAF trial and the Fire and Ice trial, are directly comparing cryoablation and RFA for AF.

**Repeat Procedures**

Repeated procedures for recurrent AF or atrial flutter were commonly performed in most of the clinical trials included in this policy statement. Of the 10 RCTs reviewed that compared RFA with medical management, only 2 did not include repeated procedures. In the other 5 studies, 1 or more repeated procedures were allowed, and success rates reported generally incorporated the results
of up to 3 procedures. In 4 studies that reported these data, repeated procedures were performed in 8.2%, 9%, 20%, and 32% of patients randomized to ablation. In their RCT of catheter ablation of AF in patients with heart failure, Hunter and colleagues report that repeat procedures were required in 65.4% of the catheter ablation group. Stabile and colleagues did not report specifics on how many patients actually underwent repeated procedures, but limited data in the publication indicated that up to 30% of treated patients were eligible for repeated procedures. In the Jais and colleagues study, patients underwent a mean of 1.8 procedures per patient and a median of 2 procedures per patient, indicating that approximately 50% of patients in the ablation group underwent at least 1 repeated procedure.

Because of this high rate of repeated procedures, the results reported in these studies do not reflect the success of a single procedure. Rather, they more accurately estimate the success of an ablation strategy that includes repeated procedures for recurrences that occur within the first year of treatment. Nonrandomized evidence suggests that early reablation increases the success of the procedure, when defined as maintenance of sinus rhythm at 1 year. There is variability in the protocol for when repeated procedures should be performed. There is also uncertainty concerning other details on repeated procedures, such as how soon after the initial procedure it should be done, the threshold of AF recurrence that should prompt a repeat, and whether medications should be tried before a repeated procedure.

Pokushalov and colleagues reported results of an RCT comparing repeat catheter ablation with antiarrhythmic drug therapy for patients with paroxysmal AF who had failed an initial pulmonary vein isolation procedure. After an initial postablation blanking period, 154 patients with symptomatic AF recurrence were randomized to drug therapy (n=77) or repeat ablation (n=77). Patients were followed for 3 years with an implanted cardiac monitor. At the 3-year follow-up, 58% (45/77) of the repeat ablation group were free from AF or atrial tachycardia on no antiarrhythmic drugs, compared with 12% (9/77) of the antiarrhythmic therapy group (p<0.01). In the antiarrhythmic drug group, 43 patients (56%) crossed over to receive repeat ablation; in the repeat ablation group, 21 patients (27%) required antiarrhythmic drug therapy. By intention-to-treat analysis, 65% (50/77) of the repeat ablation group and 45% (35/77) of the drug therapy group were free from AF or atrial tachycardia (p=0.02).

Complications

Individual clinical trials and case series report relatively low rates of complications, but may be limited in their ability to detect uncommon outcomes due to their small size. In 2013, Gupta and colleagues reported results from a systematic review and meta-analysis of periprocedural complications following catheter ablation for AF. The authors included 192 studies that included at least 100 participants undergoing catheter ablation for symptomatic AF and that reported complications. The total sample size was 83,236 patients. The overall acute complication rate was 2.9% (95% CI, 2.6 to 3.2), with significant heterogeneity across studies. The most common complications were vascular complications (1.4%), cardiac tamponade (1.0%), pericardial effusion (0.7%), stroke/transient ischemic attack (TIA) (0.6%), and pulmonary vein stenosis (0.5%).
In addition to the complication rates reported in available clinical trials and case series, there have been a number of database studies and postmarketing surveillance that report complications in larger numbers of patients than are in the clinical trials. A representative sample of these studies is discussed next, some of which were included in the Gupta and colleagues review (Shah and colleagues, Dagres and colleagues).

Waldo and colleagues reported the results of a U.S. Food and Drug Administration-directed postmarketing safety study involving 1275 patients from 6 prospective, multicenter studies of RFA using an open-irrigated catheter. A total of 4.9% (63/1275) of patients experienced any acute serious complication within 7 days of the procedure. Vascular access complications were most common, ranging from 0.5% to 4.7% across the 6 studies. Exacerbations of heart failure occurred in 1.5% of patients, and 2 patients experienced cardiac tamponade. There were no strokes or TIAs reported after the procedure.

Shah and colleagues used data from a California hospital database to evaluate complications in 4156 patients who underwent catheter ablation for AF. Major complications occurred in 5.1% (211/4156) of patients, with approximately half of these (2.6% [110/4156]) consisting of hemorrhage or hematoma at the vascular entry site. The most common cardiac complication was cardiac perforation and/or tamponade, which occurred in 2.5% (104/41156) of patients. Less common rates of serious adverse events included death (0.02%), stroke/TIA (0.31%), and pneumothorax/hemothorax (0.1%). Factors that were predictive of complications were female gender, older age, prior hospitalizations for AF, and less hospital experience with ablation.

In a study of Medicare beneficiaries, Ellis and colleagues identified 6065 admissions from 168 hospitals in which RFA for AF was performed. The total rate of in-hospital complications was 9.1%, with vascular complications accounting for over half of the total complications at a rate of 5.7%. The mortality rate was 0.4%, and 0.6% of patients suffered a stroke or TIA. Perforation or tamponade occurred in 3.1% of patients and pneumothorax occurred in 0.4% of patients. The presence of chronic obstructive pulmonary disease or unstable angina was associated with a higher risk of complications, while obesity and hyperlipidemia were associated with a lower risk. Age and hospital volume were not significant predictors of risk, but low hospital volume was a significant predictor of in-hospital death.

Complications of catheter ablation were reported in a large cohort of 1,000 patients undergoing ablation at a high-volume center in Europe. There were no deaths definitely attributable to the procedure, but there were 2 deaths of uncertain cause within the first 30 days following ablation. Overall, 3.9% of patients had a major complication resulting from the procedure. Tamponade was the most serious life-threatening complication, occurring in 1.3% of patients. Major vascular complications occurred in 1.1%. Thromboembolism, cerebrovascular accident/TIA, atrioesophageal fistula, and endocarditis were all reported complications that occurred at a rate of less than 1%.

Cappato and colleagues performed a multicenter, retrospective case series to estimate the overall mortality rate following ablation. Data were collected on 32,569 patients from 162 clinical centers worldwide. There were 32 deaths reported, for a mortality rate of 0.98 per 1000 patients. The most
common causes of death were tamponade (n=8), stroke (n=5), atrioesophageal fistula (n=5), and pneumonia (n=2).

In the MACPAF study, 1 goal was to identify adverse events, particularly cerebral thromboembolism through the use of serial magnetic resonance imaging (MRIs) and neuropsychologic testing. While there is some evidence that RFA for patients with AF improves stroke risk, a clinically significant stroke or TIA attack occurs in 0.1% to 0.8% of patients undergoing catheter ablation, and several case series have demonstrated peridural brain lesions on diffusion weighted MRI imaging in up to 18% of patients undergoing catheter ablation of the left atrium. Thus, the MACPAF investigators evaluated patients pre- and postcatheter ablation with brain MRI at 3 Tesla and neurologic and neuropsychologic testing. Short-term outcomes from these evaluations were reported by Haeusler and colleagues in 2013 and demonstrated that new ischemic lesions occurred in 41% of all patients. However, these brain lesions were not associated with cognitive dysfunction immediately after procedure. Longer-term follow-up was reported by Herm and colleagues in 2013. At follow-up MRI at 6 months after procedure, 31.3% of the acute brain lesions had formed a persistent glial scar. Similar to the short-term findings, there was no significant effect of either the ablation procedure or the presence of persistent brain lesions on attention or executive functions, short-term memory, or learning after 6 months.

Section Summary

Several large, database studies estimate the rate of adverse events from catheter ablation in the clinical care setting. The range of major adverse events in these studies is from 4 to 9%. Deaths have been reported and occur at rates less than 1%. Vascular complications at the groin site are the most common adverse events, occurring at rates of up to 5%. Serious cardiovascular adverse events such as tamponade and stroke occur uncommonly, at rates of approximately 1% or lower. There is some evidence that new ischemic lesions are commonly found on MRI after procedure, but the clinical significance of these defects is unclear.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this policy are listed in Table 1.

Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT01278953</td>
<td>A Prospective, Randomized, Multicenter, Interventional Study to Evaluate the Safety and Effectiveness of the TactiCath Percutaneous Ablation Catheter for the Treatment of Symptomatic Paroxysmal Atrial Fibrillation Using Contact Force Assisted Radiofrequency Ablation</td>
<td>400</td>
<td>Aug 2015</td>
</tr>
<tr>
<td>NCT01696136</td>
<td>Multi-electrode Pulmonary Vein Isolation Versus</td>
<td>120</td>
<td>Dec 2015</td>
</tr>
<tr>
<td>NCT</td>
<td>Study Title</td>
<td>Enrollment</td>
<td>Status</td>
</tr>
<tr>
<td>-----</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>------------</td>
<td>---------</td>
</tr>
<tr>
<td>NCT01490814^a</td>
<td>Single Tip Wide Area Catheter Ablation for PAF a Randomized Multinational Multicenter Trial (MYSTIC-PAF)</td>
<td>768</td>
<td>Jun 2016</td>
</tr>
<tr>
<td>NCT01420393</td>
<td>A Controlled, Prospective, Non-Inferiority, Parallel-Group, Randomised, Interventional, Open, Blinded Outcome Assessment (PROBE-Design), Multi-centre Trial, Comparing Efficacy and Safety of Isolation of the Pulmonary Veins With a Cryoballoon Catheter Versus a Radiofrequency Ablation With a ThermoCool Catheter in Patients With Paroxysmal Atrial Fibrillation</td>
<td>600</td>
<td>Sep 2016</td>
</tr>
<tr>
<td>NCT01687166α</td>
<td>Clinical Evaluation of the Blazer Open-Irrigated Ablation Catheter for the Treatment of Paroxysmal Atrial Fibrillation (ZERO-AF)</td>
<td>552</td>
<td>Dec 2016</td>
</tr>
<tr>
<td>NCT02274857α</td>
<td>Randomized Evaluation of Atrial Fibrillation Rhythm Control Versus Rate Control Trial in Patients With Heart Failure and High Burden Atrial Fibrillation</td>
<td>200</td>
<td>Jun 2017</td>
</tr>
<tr>
<td>NCT02150902</td>
<td>Augmented Wide Area Circumferential Catheter Ablation for Reduction of Atrial Fibrillation Recurrence (AWARE)</td>
<td>342</td>
<td>Dec 2017</td>
</tr>
<tr>
<td>NCT02106663</td>
<td>Evaluating the Efficacy of Circumferential Pulmonary Vein Ablation (CPVA) Versus Segmental Pulmonary Vein Isolation (SPVI) in Paroxysmal Atrial Fibrillation</td>
<td>100</td>
<td>Dec 2017</td>
</tr>
<tr>
<td>NCT00911508</td>
<td>Catheter Ablation vs Anti-arrhythmic Drug Therapy for Atrial Fibrillation Trial (CABANA)</td>
<td>2200</td>
<td>Jun 2018</td>
</tr>
<tr>
<td>Unpublished</td>
<td>Focal Impulse and Rotor Modulation Ablation Trial for Treatment of Paroxysmal Atrial Fibrillation (FIRMAT-PAF)</td>
<td>1</td>
<td>Terminated</td>
</tr>
</tbody>
</table>

NCT: national clinical trial
^a Denotes industry-sponsored or cosponsored trial.

**Clinical Input Received from Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

**2011 Input**
In response to requests, input was received from 2 physician specialty societies (3 reviewers) and 2 academic medical centers while this policy was under review in 2011. While the input was mixed, there was general agreement with the policy statements. One reviewer commented that use of cryoablation may have a specific role when ablation targets are close to the AV node.

**2015 Input**

In response to requests, input was received from 3 physician specialty societies (6 reviewers) and 4 academic medical centers while this policy was under review in 2015. Input was focused on the use of ablation as an initial procedure for symptomatic paroxysmal and persistent AF and on the use of cryoablation for AF. There was consensus supporting the use of RFA as an initial treatment for symptomatic paroxysmal AF, and the use of cryoablation as an alternative to RFA as treatment for AF. For the use of RFA as initial treatment for symptomatic persistent AF, support from clinical input was more mixed.

**Practice Guidelines and Position Statements**

An expert consensus document on catheter and surgical catheter ablation for AF was developed jointly by 7 cardiac specialty societies (Heart Rhythm Society [HRS], European Heart Rhythm Association, European Cardiac Arrhythmia Society, American College of Cardiology [ACC], American Heart Association [AHA], Asia Pacific Heart Rhythm Society, Society of Thoracic Surgeons) in 2012. The following recommendations were made concerning indications for catheter ablation:

- Symptomatic AF [atrial fibrillation] refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication
  - Paroxysmal: Catheter ablation is recommended (Class I recommendation, Level of evidence A)
  - Persistent: Catheter ablation is reasonable (Class IIa recommendation, Level of evidence B)
  - Longstanding Persistent: Catheter ablation may be considered (Class IIb recommendation, Level of evidence B)
- Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent
  - Paroxysmal: Catheter ablation is reasonable (Class IIa recommendation, Level of evidence B)
  - Persistent: Catheter ablation may be considered (Class IIb recommendation, Level of evidence C)
  - Longstanding Persistent: Catheter ablation may be considered (Class IIb recommendation, Level of evidence C)

In 2006, ACC/AHA/HRS published an update to their practice guidelines for the treatment of AF. These guidelines reflect the results of the rate- versus rhythm-controlled randomized studies. Explicit recommendations are classed as I, IIa, IIb, or III. Class IIa is defined as: “the weight of
evidence or opinion is in favor of the procedure or treatment.” The recommendations are further classified according to the type of data available. Class C data are defined as “expert consensus.”

The guidelines describe the use of ablation of the pulmonary vein (PV) and note that the “...technique of ablation has continued to evolve from early attempts to target individual ectopic foci within the PV to circumferential electrical isolation of the entire PV musculature.” Two specific recommendations regarding the use of catheter ablation were judged class IIa. These are (1) “It is reasonable to use ablation of the AV node or accessory pathway to control heart rate when pharmacological therapy is insufficient or associated with side effects. (Level of Evidence: B); and (2) “Catheter ablation is a reasonable alternative to pharmacological therapy to prevent recurrent AF in symptomatic patients with little or no LA [left atrial] enlargement. (Level of Evidence: C).” “Catheter ablation of the accessory pathway is recommended in symptomatic patients with AF who have WPW [Wolff-Parkinson-White] syndrome, particularly those with syncope due to rapid heart rate of those with a short bypass tract refractory period. (Level of Evidence: B)”

- Catheter ablation without prior medical therapy to control AF. (Class III, Level of Evidence C).

In 2014, the ACC/AHA Task Force on Practice Guidelines and HRS issued guidelines for the management of patients with atrial fibrillation.

The guidelines included the following recommendations for rate control:

- Class I Recommendations:
  - AV nodal ablation with permanent ventricular pacing is reasonable to control heart rate when pharmacological therapy is inadequate and rhythm control is not achievable. (Level of evidence: B)
- Class III Recommendations (Harm):
  - Harm AV nodal ablation with permanent ventricular pacing should not be performed to improve rate control without prior attempts to achieve rate control with medications. (Level of evidence: C)

The guidelines included the following recommendations for rhythm control:

- Class I:
  - AF catheter ablation is useful for symptomatic paroxysmal AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm-control strategy is desired. (Level of Evidence: A)
  - Before consideration of AF catheter ablation, assessment of the procedural risks and outcomes relevant to the individual patient is recommended. (Level of Evidence: C)
- Class IIa:
AF catheter ablation is reasonable for some patients with symptomatic persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication. (Level of Evidence: A)

In patients with recurrent symptomatic paroxysmal AF, catheter ablation is a reasonable initial rhythm-control strategy before therapeutic trials of antiarrhythmic drug therapy, after weighing the risks and outcomes of drug and ablation therapy. (Level of Evidence: B)

- Class IIb:
  o AF catheter ablation may be considered for symptomatic long-standing (>12 months) persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm-control strategy is desired. (Level of Evidence: B)
  o AF catheter ablation may be considered before initiation of antiarrhythmic drug therapy with a class I or III antiarrhythmic medication for symptomatic persistent AF when a rhythm-control strategy is desired. (Level of Evidence: C)

- Class III: Harm:
  o AF catheter ablation should not be performed in patients who cannot be treated with anticoagulant therapy during and after the procedure. (Level of Evidence: C)
  o AF catheter ablation to restore sinus rhythm should not be performed with the sole intent of obviating the need for anticoagulation. (Level of Evidence: C)

Although the guidelines’ authors do not make a specific recommendation about the use of cryoablation, they state, “Cryoballoon ablation is an alternative to point-by-point radiofrequency ablation to achieve pulmonary vein isolation.”

The American College of Physicians and American Academy of Family Physicians issued clinical practice guidelines in 2003 for patients with new-onset AF, which were reaffirmed in 2008. These guidelines state most patients with new-onset AF should be treated with a pharmacologic rate control strategy and long-term anticoagulation. Similar to ACC/AHA guidelines, this document does not include specific recommendations for catheter-based ablation techniques in their treatment algorithms.

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.
VI. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VII. References

8. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Catheter ablation of the pulmonary veins as a treatment for atrial fibrillation. TEC Assessments 2008; Volume 23 Tab 11.


63. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society. Heart Rhythm. Apr 2012; 9(4):632-696 e621.


