

Medical Policy



Title: Radiofrequency Catheter Ablation of the Pulmonary Veins as Treatment for Atrial Fibrillation

Professional

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DESCRIPTION

Radiofrequency ablation using a percutaneous catheter-based approach is widely used to treat supraventricular arrhythmias. Atrial fibrillation 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 radiofrequency ablation and cryoablation, is being studied in the treatment of various types of atrial fibrillation.

Atrial fibrillation is the most common cardiac arrhythmia, with a prevalence estimated at 0.4% of the population, increasing with age. The underlying mechanism of atrial fibrillation involves an 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 atrial fibrillation appears to be located within the cardiac muscle that extends into the pulmonary veins.

Atrial fibrillation accounts for approximately one-third of hospitalizations for cardiac rhythm disturbances. Symptoms of atrial fibrillation, i.e., palpitations; decreased exercise tolerance; and 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 atrial fibrillation are at higher risk for stroke, and anticoagulation is typically recommended. Atrial fibrillation is also associated with other cardiac conditions, such as valvular heart disease, heart failure, hypertension, and diabetes. Although episodes of atrial fibrillation can be converted to normal sinus rhythm using either pharmacologic or electroshock conversion, the natural history of atrial fibrillation is one of recurrence, thought to be related to fibrillation-induced anatomic and electrical remodeling of the atria.

Atrial fibrillation 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 re-establish and maintain normal sinus rhythm. Rhythm control has long been considered an important treatment goal for management of atrial fibrillation, 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 to rate control.

Currently, the main indications for a rhythm control are for patients with paroxysmal or persistent atrial fibrillation who have hemodynamic compromise associated with episodes of atrial fibrillation 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 atrial fibrillation are typical, and patients with persistent atrial fibrillation may require multiple episodes of cardioversion. Implantable atrial defibrillators, which are designed to detect and terminate an episode of atrial fibrillation, are an alternative in patients otherwise requiring serial

cardioversions, but these have not yet achieved widespread use. Patients with paroxysmal atrial fibrillation, by definition, do not require cardioversion but may be treated pharmacologically to prevent further arrhythmic episodes.

Treatment of permanent atrial fibrillation 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 atrial fibrillation.

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 atrial fibrillation 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 (i.e., valve repair), is an ablative procedure that involves sequential atriotomy incisions designed to create electrical barriers that prevent the maintenance of atrial fibrillation. 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.

Radiofrequency ablation 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 atrial fibrillation, since 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 atrial fibrillation. In the late 1990s, it was recognized that atrial fibrillation 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 is the most commonly used approach at the present time. The procedure also can be done using cryoablation technology.

Repeat procedures following an initial radiofrequency ablation are commonly performed if atrial fibrillation recurs or if atrial flutter develops post-procedure. The need for repeat procedures may, in part, depend on clinical characteristics of the patient (age, persistent vs. paroxysmal atrial fibrillation, atrial dilatation, etc.), 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 atrial fibrillation ablation procedure. A number of clinical and demographic factors have been associated with the need for a second procedure, including age, length of atrial fibrillation, permanent atrial fibrillation, 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 Inc.) were approved by the U.S. Food and Drug Administration (FDA) through the pre-market 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 atrial fibrillation, when used with compatible three-dimensional electroanatomic mapping systems." (For radiofrequency ablation)

In December 2010, Medtronic's Arctic Front® Cardiac CryoAblation Catheter and CryoConsole were approved by the 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, the FDA has also granted PMA approval to numerous catheter ablation systems for other ablation therapy for arrhythmias such as supraventricular tachycardia, atrial flutter, and ventricular tachycardia.

POLICY

Transcatheter radiofrequency ablation of arrhythmogenic foci is considered **medically necessary** as a treatment of atrial fibrillation when the patient:

1. Has markedly symptomatic paroxysmal or persistent atrial fibrillation, and
2. Is resistant to one or more antiarrhythmic drugs (or has intolerance or a contraindication to appropriate antiarrhythmic drug therapy).

Policy Guidelines

1. Prior to 2013, there is was no specific CPT code for pulmonary vein ablation. CPT code 93651 would have been used. Code 93651 included ablation of an intra-atrial arrhythmogenic focus as treatment of a supraventricular tachycardia. Circumferential ablation of the pulmonary vein might be considered basically intra-arterial in location due to its close proximity to the pulmonary os and atria. Supraventricular tachycardias typically describe arrhythmias due to accessory pathways within the atria, such as Wolff-Parkinson-White syndrome or atrioventricular nodal reentry arrhythmias. Although not consistently associated with tachycardia, strictly speaking atrial fibrillation could be considered a type of supraventricular tachycardia.
2. As many as 30% of patients will require a follow-up (repeat) procedure because of recurrence of atrial fibrillation or 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.

RATIONALE

In patients with paroxysmal or persistent atrial fibrillation, pulmonary vein ablation may be considered an alternative to drug therapy. (1) In patients with permanent atrial fibrillation, pulmonary vein ablation may be considered an alternative to drug therapy or to atrioventricular (AV) nodal ablation and pacing. (2) For all types of atrial fibrillation, it is possible that pulmonary vein 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 atrial fibrillation, which underlies the evaluation of evidence on catheter ablation. Randomized trials of pharmacologic therapies have not demonstrated the superiority of rhythm versus rate control. (3-5) However, the apparent equivalency of these two 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, that 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 atrial fibrillation

A variety of outcomes for treatment of atrial fibrillation may be considered. (6) The mortality and morbidity related to atrial fibrillation, 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 atrial fibrillation, such as symptoms and reduced exercise tolerance. Atrial fibrillation 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 atrial fibrillation.

Recurrence of atrial fibrillation is a more problematic outcome measure, since the intermittent and often transient nature of recurrences makes accurate measurement difficult. (6) 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 atrial fibrillation recurrence and recommends a measure of atrial fibrillation “burden,” defined as the percentage of time an individual is in atrial fibrillation, as the optimal measure of treatment efficacy. (6) 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 atrial fibrillation treatment were included in the 2006 American College of Cardiology/American Heart Association practice guidelines for the treatment of atrial fibrillation. (7) These guidelines pointed out that the appropriate endpoints for evaluation of treatment efficacy in patients with paroxysmal or persistent atrial fibrillation have little in common. For example, in studies of persistent atrial fibrillation, the proportion of patients in sinus rhythm at the end of follow-up is a useful endpoint, but this is a less useful measure in studies of paroxysmal atrial fibrillation. Given all these variables, ideally, controlled clinical trials would report a range of outcomes (including QOL) and complications in homogeneous patient groups and compare to the most relevant treatment alternatives, such as pharmacologic therapy; defibrillator therapy; and AV nodal ablation, depending on the classification of atrial fibrillation (paroxysmal, persistent, or permanent).

Radiofrequency ablation of the pulmonary veins

Systematic Reviews

The literature review for this policy was originally based on a 2008 TEC Assessment. (8) Six randomized, controlled trials (RCTs) met the inclusion criteria for this TEC Assessment. (9-14) 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 atrial fibrillation, as a first-line treatment option (n=1 trial (14)); 2) patients with symptomatic paroxysmal or persistent atrial fibrillation who have failed treatment with antiarrhythmic drugs (n=4 trials (9, 11-13)); and 3) patients with symptomatic atrial fibrillation 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 (10)).

All 6 trials reported that maintenance of sinus rhythm was improved for the catheter ablation group. Recurrence rates of atrial fibrillation at 1 year ranged from 11–44% for the catheter ablation groups in these trials, compared with 63–96% for the medication groups. Four of the 6 trials reported QOL outcomes. One of these (11) only reported within-group comparisons, as opposed to between-group comparisons. The other 3 trials (9, 10, 14) reported improvements in QOL associated with catheter ablation. These QOL measures were self-reported, and since 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 atrial fibrillation. The Assessment concluded that radiofrequency catheter ablation is more effective than medications in maintaining sinus rhythm across a wide

spectrum of patients with atrial fibrillation 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 atrio-esophageal 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 1–5% range.

Based on these findings, TEC criteria were met for 2 indications: patients with symptomatic paroxysmal or persistent atrial fibrillation who have failed treatment with antiarrhythmic drugs and patients with symptomatic atrial fibrillation 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 recurrent atrial fibrillation for this population will reduce or eliminate the symptoms associated with episodes of atrial fibrillation. For the other indication, the single multicenter RCT available was judged sufficient to conclude that catheter ablation improved outcomes compared to 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, and maintenance of sinus rhythm.

A Cochrane Review on catheter ablation for paroxysmal and persistent atrial fibrillation was published in 2012. (15) This review included 7 RCTs of catheter ablation versus medical therapy. Main conclusions were that catheter ablation was superior at reducing the recurrence of atrial fibrillation (RR 0.27, 95% CI 0.18-0.41), but that there were no differences in mortality (RR 0.50, 95% CI 0.04-5.65), embolic complications (RR 1.01, 95% CI 0.18-5.68), or death from thromboembolism (RR 3.04, 95% CI 0.13-73.4).

Two systematic reviews published in 2008 (16, 17) 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. (11-14) Noheria et al. (17) included 3 of these 4 RCTs, (12-14) as well as an additional small RCT of 30 patients not included in the TEC Assessment. (18) Gjesdal et al. (16) included 5 RCTs in their analysis, including the 4 trials in the Noheria et al. systematic review, and 1 additional trial (included in the TEC Assessment) that compared catheter ablation plus antiarrhythmic drugs with antiarrhythmic drugs alone. (11)

Both of these systematic reviews concluded that catheter ablation was more effective than pharmacologic treatment in maintaining normal sinus rhythm. In combined analysis, Noheria et al. (17) reported atrial-fibrillation-free survival at 1 year to be 75.7% in the catheter ablation group compared to 18.8% in the comparison group. The relative risk for maintaining sinus rhythm was 3.73 (95% confidence interval [CI]: 2.47–5.63) for the catheter-ablation group compared to alternative treatment. Gjesdal et al. (16) concluded that the available evidence was of moderate quality and consistent in reporting that atrial-fibrillation-free survival was superior for the catheter ablation group. However, due to unexplained heterogeneity, these authors did not perform a combined analysis.

Additional RCTs

Since the TEC Assessment, three additional RCTs comparing radiofrequency ablation (RFA) versus pharmacologic treatment have been identified. Wilber et al. (19) enrolled 167 patients who had failed at least one antiarrhythmic medication and had at least 3 atrial fibrillation 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 atrial fibrillation compared to 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 et al. (20) randomly assigned 70 patients with type 2 diabetes and atrial fibrillation to either radiofrequency ablation or an antiarrhythmic medication. Follow-up was for 1 year, with the primary outcome being recurrence of atrial fibrillation. At the end of the trial, 42.9% of patients in the medication group were free of atrial fibrillation compared to 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).

Nielsen et al. published an RCT of RFA ablation as the initial therapy for paroxysmal atrial fibrillation in 2012. (21) 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 atrial fibrillation (percent of time in atrial fibrillation on holter monitor) at each time point and cumulative burden of atrial fibrillation over all time points. For the individual time points, the burden of atrial fibrillation 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 to pharmacologic therapy (90th percentile of cumulative burden, 13% versus 19%, $p=0.10$). The secondary outcome of percent of patients free from atrial fibrillation 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 atrial fibrillation (93% vs. 84%, $p=0.01$). There was one death in the ablation group due to a procedural-related stroke, and there were 3 patients in the ablation group who developed cardiac tamponade following the procedure.

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 20-30%, requiring repeat ablations. Rates of longer-term recurrence are lower if early recurrence does not occur, in the range of 1-2% per year.

Hussein et al. (22) 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 atrial fibrillation. 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.

Several smaller studies have also reported longer-term follow-up. Weerasooriya et al. (21) 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 post-ablation, arrhythmia-free survival was 87%, 81%, and 63%. Tzou et al. (23) reported long-term follow-up for 123 patients who had a previous successful ablation, defined as free of atrial fibrillation at 1 year. At 3 years of follow-up, 85% of patients were still free of atrial fibrillation and off of all medications, and at 5 years, 71% remained free of atrial fibrillation. The authors estimated a late recurrence rate of approximately 7% per year for patients with an initial successful procedure. In a similar study, Bertaglia et al. (24) 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 atrial fibrillation 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 atrial fibrillation. Sawhney et al. (25) reported 5-year success rates in 71 patients who underwent ablation in 2002 or 2003. Freedom from symptomatic atrial fibrillation 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 post-ablation.

Conclusions:

Numerous RCTs of RFA of the pulmonary veins versus medical management report that freedom from atrial fibrillation at 1 year is higher with RFA compared to medical management. The trials mainly include patients who have failed anti-arrhythmic medications, although 2 trials treat patients with paroxysmal atrial fibrillation as initial treatment. These studies report that a majority of patients undergoing RFA are free of atrial fibrillation at 1 year. Quality of life 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 atrial fibrillation. Larger RCTs are underway to evaluate long-term clinical outcomes such as stroke and mortality.

Cryoablation of the pulmonary veins

A number of studies reported outcomes of ablation using cryoablation. These were mainly case series (26, 27) reporting success rates in the range of that reported for radiofrequency ablation. One small matched analysis compared 20 patients undergoing cryoablation with 20 patients undergoing radiofrequency ablation, matched for age, gender, left ventricular ejection fraction, and atrial fibrillation history. (28) Freedom from atrial fibrillation at 6 months was 55% for the cryoablation group, compared to 45% for the radiofrequency ablation group, a difference that was not significantly different.

Results of the STOP-AF trial, an RCT of cryoablation versus antiarrhythmic medications, were presented at the March 2010 American College of Cardiology meeting, but as of February 2012, results have not yet been published in the peer-reviewed literature. (29) This study enrolled 245 patients with paroxysmal atrial fibrillation who had failed a median of 1.2 medications. At 1-year follow-up, 69.9% of patients in the ablation group were free of atrial fibrillation versus 7.3% in the medication group. There was also a significantly greater reduction in symptoms for the ablation group. Serious adverse events were reported in 3.1%

of ablation patients. Phrenic nerve injury occurred at a rate of 13.5%, with 86% resolved at 12 months.

A meta-analysis of studies of cryoablation was published in 2011. (30) This analysis included the STOP-AF results in abstract form and a total of 22 other non-randomized 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 atrial fibrillation, were 73% (95% CI: 69-77%) for paroxysmal atrial fibrillation and 60% (95% CI: 54-66%) for persistent atrial fibrillation. 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%).

There are ongoing trials of cryoablation versus RFA for atrial fibrillation. The FreezeAF trial (30) is a randomized controlled noninferiority trial comparing cryoablation to RFA for patients with paroxysmal atrial fibrillation. Enrollment of 244 patients is planned, and patients will be followed for at least 1 year. The primary outcome is freedom from atrial fibrillation off all drugs. Secondary outcomes include longer-term success rates, procedural data, and cost-effectiveness. The MACPAF trial (31) will compare outcomes of RFA and cryoablation in 108 patients with paroxysmal atrial fibrillation, with a focus on adverse events including cerebral thromboembolism through the use of serial MRIs and neuro-psychological testing.

Conclusions:

Numerous case series of cryoablation report uncontrolled outcomes of this technique. One RCT of cryoablation versus medical management has been completed and is available in abstract form; this trial reports freedom from atrial fibrillation that is in the range of results reported for RFA, but on the low side. Similar types of complications are reported following cryoablation as compared to RFA, but the available evidence is not sufficient to conclude whether rates of adverse events are reduced with cryoablation. Therefore, the evidence is not sufficient to determine the comparative efficacy of cryoablation compared to RFA. Ongoing RCTs are currently addressing this question.

Repeat procedures

Repeated procedures for recurrent atrial fibrillation or atrial flutter were commonly performed in most of the clinical trials included in this policy statement. Of the 7 RCTs reviewed, only 2 (14, 20) did not include repeated procedures. In the other 5 studies, one or more repeated procedures were allowed, and success rates reported generally incorporated the results of up to 3 procedures. In 3 studies that reported these data, repeated procedures were performed in 9%, (12) 20%, (10) and 32% (11) of patients randomized to ablation. Stabile et al. (13) 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 et al. study, (9) 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 one 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. (32) 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 atrial fibrillation recurrence that should prompt a repeat, and whether medications should be tried prior to a repeated procedure. (32)

Complications

In addition to the complication rates reported in available clinical trials and case series, there have been a number of database studies and post-marketing surveillance that report complications in larger numbers of patients than are in the clinical trials. A representative sample of these studies is discussed below.

Waldo et al. reported the results of an FDA-directed post-marketing safety study involving 1275 patients from six prospective, multicenter studies of RFA ablation using an open-irrigated catheter. (33) A total of 4.9% (63/1275) of patients experienced any acute serious complication within seven days of the procedure. Vascular access complications were most common, ranging from 0.5% to 4.7% across the six studies. Exacerbations of heart failure occurred in 1.5% of patients and two patients experienced cardiac tamponade. There were no strokes or TIA's reported post-procedure.

Shah et al. (34) used data from a California hospital database to evaluate complications in 4,156 patients who underwent catheter ablation for atrial fibrillation. Major complications occurred in 5.1% (211/4,156) of patients, with approximately half of these (2.6%, 110/4,156) 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% (104/4,156) 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 atrial fibrillation, and less hospital experience with ablation.

In a study of Medicare beneficiaries, Ellis et al. (22) identified 6,065 admissions from 168 hospitals in which RFA for atrial fibrillation 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 transient ischemic attack (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 (COPD) 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. (35) 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/transient ischemic attack, atrio-esophageal fistula, and endocarditis were all reported complications that occurred at a rate of less than 1%.

Cappato et al. (36) 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 1,000 patients. The most common causes of death were tamponade (n=8), stroke (n=5), atrio-esophageal fistula (n=5), and pneumonia (n=2).

Conclusions:

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 4-9%. 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.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

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 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. 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.

Summary

Results of randomized, controlled trials that compare radiofrequency ablation with antiarrhythmic medications report that freedom from atrial fibrillation 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 atrial fibrillation at 1 year. However, the majority of patients who are atrial-fibrillation-free at 1 year remain atrial-fibrillation-free at 5 to 6 years. Rates of complications following ablation remain uncertain; evidence for this update supports a serious complication rate in the range of 4-9% and a mortality rate of less than 1%. As a result, radiofrequency ablation of the pulmonary veins is considered medically necessary for symptomatic paroxysmal or persistent atrial fibrillation, when antiarrhythmic medications have failed to adequately control symptoms.

Case series of cryoablation report success rates in the range seen for radiofrequency ablation, and the preliminary results of one randomized, controlled trial report that cryoablation is more effective than medications. However, rates of success with cryoablation are on the lower end of results seen when using radiofrequency. It is not yet possible to determine whether outcomes of cryoablation are similar to that for radiofrequency ablation. Randomized, controlled trials comparing the two techniques are currently underway. Thus, cryoablation of the pulmonary veins is considered investigational.

Repeat procedures are commonly 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 to the initial ablation, targeting specific areas where ablation may not be complete, and/or a focused ablation for treatment of post-ablation atrial flutter. These repeat procedures, generally up to 2 repeat ablations, may therefore be considered medically necessary.

Practice Guidelines and Position Statements

An expert consensus document on catheter and surgical catheter ablation for atrial fibrillation was developed jointly by seven cardiac specialty societies (HRS, EHRA, ECAS, ACC, AHA, APHRS, STS) in 2012. (37) The following recommendations were made concerning indications for catheter ablation:

- Symptomatic AF 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, the American College of Cardiology published an update to their practice guidelines for the treatment of atrial fibrillation. These guidelines reflect the results of the rate versus rhythm controlled randomized studies. (7) 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 [atrial fibrillation] in symptomatic patients with little or no [left atrial] enlargement. (Level of Evidence: C)."

The guidelines also encourage further research in this area given uncertainties in patient populations, technique, and outcome assessment. The authors state that “despite these advances, the long-term efficacy of catheter ablation to prevent recurrent [atrial fibrillation] requires further study.”

The American College of Physicians and American Academy of Family Physicians issued clinical practice guidelines in 2003 for patients with new-onset atrial fibrillation. (38) These guidelines state the majority of patients with new-onset atrial fibrillation should be treated with a pharmacologic rate control strategy and long-term anticoagulation. Similar to the American College of Cardiology/American Heart Association guidelines, this document does not include specific recommendations for catheter-based ablation techniques in their treatment algorithms.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

- 93653 Comprehensive electrophysiologic evaluation including insertion and repositioning of multiple electrode catheters with induction or attempted induction of an arrhythmia with right atrial pacing and recording, right ventricular pacing and recording, His recording with intracardiac catheter ablation of arrhythmogenic focus; with treatment of supraventricular tachycardia by ablation of fast or slow atrioventricular pathway, accessory atrioventricular connection, cavo-tricuspid isthmus or other single atrial focus or source of atrial re-entry
- 93654 Comprehensive electrophysiologic evaluation including insertion and repositioning of multiple electrode catheters with induction or attempted induction of an arrhythmia with right atrial pacing and recording, right ventricular pacing and recording, His recording with intracardiac catheter ablation of arrhythmogenic focus; with treatment of supraventricular tachycardia by ablation of fast or slow atrioventricular pathway, accessory atrioventricular connection, cavo-tricuspid isthmus or other single atrial focus or source of atrial re-entry: with treatment of ventricular tachycardia or focus of ventricular ectopy including intracardiac electrophysiologic 3D mapping, when performed, and left ventricular pacing and recording, when performed.
- 93655 Intracardiac catheter ablation of a discrete mechanism of arrhythmia which is distinct from the primary ablated mechanism, including repeat diagnostic maneuvers, to treat a spontaneous or induced arrhythmia
- 93656 Comprehensive electrophysiologic evaluation including transeptal 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.
- 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

93799 Unlisted cardiovascular service or procedure

DIAGNOSIS

- 427.31 Atrial fibrillation
- 427.32 Atrial flutter
- 428.0 Congestive heart failure, unspecified

ICD-10 DIAGNOSIS (Effective October 1, 2014)

- I48.1 Persistent atrial fibrillation
- I48.2 Chronic atrial fibrillation
- I50.21 Acute systolic (congestive) heart failure
- I50.22 Chronic systolic (congestive) heart failure
- I50.23 Acute on chronic systolic (congestive) heart failure
- I48.3 Typical atrial flutter
- I50.31 Acute diastolic (congestive) heart failure
- I50.32 Chronic diastolic (congestive) heart failure
- I50.33 Acute on chronic diastolic (congestive) heart failure
- I48.4 Atypical atrial flutter
- I50.41 Acute combined systolic (congestive) and diastolic (congestive) heart failure
- I50.42 Chronic combined systolic (congestive) and diastolic (congestive) heart failure
- I50.43 Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure

REVISIONS

03-30-2007	Previously this policy was an Experimental / Investigational policy under the title of Pulmonary Vein Isolation and Ablation as a Treatment of Atrial Fibrillation. The guideline changed on 03/30/07 considering the procedure medically necessary at the approval of the Medical Director with specific guidelines.
05-2-2007	The guideline was approved by Cardiology Liaison Committee with removal of the 93651 CPT code. The Medical Director approved the policy for placement on the web site.
11-17-2007	<p>Changed Title From: "Transcatheter Radiofrequency Ablation as a Treatment of Atrial Fibrillation"</p> <p>To: "Radiofrequency Catheter Ablation of the Pulmonary Veins as Treatment for Atrial Fibrillation"</p> <p>Added Description section.</p> <p>In Policy Section:</p> <ul style="list-style-type: none"> ▪ Liberalized #2 to require "Is resistant to one or more antiarrhythmic drugs..." instead of two or more antiarrhythmic drugs.
01-26-2010	<p>Title:</p> <ul style="list-style-type: none"> ▪ Changed From: Transcatheter Radiofrequency Ablation as a Treatment of Atrial Fibrillation To: Radiofrequency Catheter Ablation of the Pulmonary Veins as Treatment for Atrial Fibrillation <p>Description Section updated.</p> <p>In Policy Section:</p> <ul style="list-style-type: none"> ▪ Liberalized #2 requiring "one or more antiarrhythmic drugs" rather than "two or

	more antiarrhythmic drugs"
	Added Rationale Section
	Updated References Section
10-08-2010	In policy section: <ul style="list-style-type: none"> ▪ Remove "in the pulmonary vein" to read "Transcatheter radiofrequency ablation of arrhythmogenic foci is considered medically necessary as a treatment of atrial fibrillation when the patient..."
	In Rationale Section: <ul style="list-style-type: none"> ▪ Added August 2010
	Updated Reference Section <ul style="list-style-type: none"> ▪ Added references 19-26
	Updated Other References Section: <ul style="list-style-type: none"> ▪ Added Blue Cross and Blue Shield of Kansas Cardiology Liaison Committee, April 2010
03-28-2011	Description section updated.
	Reference section updated.
	Reference section updated.
06-06-2011	Incorrect effective date noted and corrected. Removed "January 26, 2010" and inserted correct effective dates "October 8, 2010" for the Professional side, "November 8, 2010" for the Institutional side.
08-24-2012	Description section updated.
	Rationale section updated.
	Reference section updated.
01-15-2013	In the Coding section: <ul style="list-style-type: none"> ▪ Removed CPT codes: 93651 (Effective 12-31-2012) ▪ Added new CPT codes: 93653, 93654, 93655, 93656, 93657 (Effective 01-01-2013)
06-14-2013	Rational section updated.
	Reference section updated.
	In Coding section: <ul style="list-style-type: none"> ▪ Added ICD-10 Diagnosis codes (<i>Effective October 1, 2014</i>)

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