Open and Thoracoscopic Approaches to Treat Atrial Fibrillation and Atrial Flutter (Maze and Related Procedures)

Description

There are a variety of surgical approaches to treat atrial fibrillation (AF) that work by interrupting abnormal electrical activity in the atria. Open surgical procedures, such as the Cox-Maze procedure were first developed for this purpose, and are now generally performed in conjunction with valvular or coronary artery bypass graft (CABG) surgery. Surgical techniques have evolved to include minimally invasive approaches that use epicardial radiofrequency ablation (RFA) a thoracoscopic or mediastinal approach and hybrid catheter ablations/open procedures.

Background

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia, characterized by disorganized atrial activation with ineffective atrial ejection. 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. The atria are frequently abnormal in patients with AF and demonstrate enlargement or increased conduction time. Atrial flutter is a variant of atrial fibrillation.

The first-line treatment for AF usually includes medications to maintain sinus rhythm and/or control the ventricular rate. Antiarrhythmic medications are only partially effective; therefore, medical treatment is not sufficient for many patients. Percutaneous catheter ablation, using endocardial ablation, is an accepted second-line treatment for patients who are not adequately controlled on medications. Catheter ablation is successful in maintaining sinus rhythm for a majority of patients, but long-term recurrences are common and increase over time. Surgical ablation, performed either by open surgical techniques or thoracoscopy, is an alternative approach to percutaneous catheter ablation.

Open surgical techniques: The classic Cox-Maze III procedure is a complex surgical procedure that involves sequential atriotomy incisions that interrupt the aberrant atrial conduction pathways in the heart for patients with AF. The procedure is also intended to preserve atrial pumping function. It is indicated for patients who do not respond to medical or other surgical antiarrhythmic therapies and is
often performed in conjunction with correction of structural cardiac conditions such as valve repair or replacement. This procedure is considered the criterion standard for surgical treatment of drug-resistant AF with an approximately 90% success rate.

The maze procedure entails making incisions in the heart that:

- direct an impulse from the sinoatrial (SA) node to the atrioventricular (AV) node;
- preserve activation of the entire atrium; and
- block re-entrant impulses that are responsible for AF or atrial flutter.

The classic Cox-Maze procedure is performed on a non-beating heart during cardiopulmonary bypass. Simplification of the maze procedure has evolved with the use of different ablation tools such as microwave, cryotherapy, ultrasound, and radiofrequency (RF) energy sources to create the atrial lesions instead of employing the incisional technique used in the classic maze procedure.

**Minimally invasive (thoracoscopic) techniques**: In addition, less invasive, transthoracic, endoscopic, off-pump procedures to treat drug-resistant AF are being developed. The evolution of these procedures involves both different surgical approaches and different lesion sets. Alternative surgical approaches include mini-thoracotomy, and total thoracoscopy with video assistance. Open thoracotomy and mini-thoracotomy employ cardiopulmonary bypass and open heart surgery, while thoracoscopic approaches are performed on the beating heart. Thoracoscopic approaches do not enter the heart and use epicardial ablation lesion sets, whereas the open approaches use either the classic “cut and sew” approach or endocardial ablation.

Lesion sets may vary independent of the surgical approach, with a tendency toward less extensive lesion sets targeted to areas that are most likely to be triggers of AF. The most limited lesion sets involve pulmonary vein isolation and exclusion of the left atrial appendage. More extensive lesion sets include linear ablations of the left and/or right atrium and ablation of ganglionic plexi. Some surgeons perform left-atrial reduction in cases of left-atrial enlargement.

The type of energy used for ablation also varies; RF energy is most commonly applied. Other types of energy sources such as cryoablation and high-intensity ultrasound have also been used. For the purposes of this policy statement, the variations on surgical procedures for AF will be combined under the heading of ‘modified maze’ procedures.

**Hybrid techniques**: “Hybrid” ablation refers to a procedure that utilizes both thoracoscopic and percutaneous approaches in the same patient. Ablation is performed on the outer surface of the heart (epicardial) via the thoracoscopic approach, and on the inner surface of the heart (endocardial) via the percutaneous approach. The rationale for doing a hybrid procedure is that a combination of both techniques may result in more complete ablation. Thoracoscopic epicardial ablation is limited by the inability to perform all possible ablation lines, since the posterior portions of the heart are not accessible via thoracoscopy. Percutaneous, endoscopic ablation is limited by incomplete ablation lines that often require repeat procedures. By combining both procedures, a full set of ablation lines can be performed, and incomplete ablation lines can be minimized.
The hybrid approach first involves thoracoscopy with epicardial ablation. Following this procedure, an electrophysiologic study is performed percutaneously followed by endocardial ablation as directed by the results of electrophysiology. Most commonly, the electrophysiology study and endocardial ablation are done immediately after the thoracoscopy as part of a single procedure. However, some hybrid approaches perform the electrophysiology study and endocardial ablation, as directed by the electrophysiology study, on a separate day.

**Regulatory Status**

Several RFA systems that are used for cardiac tissue ablation have been cleared for marketing by FDA based on substantial equivalence to predicate devices. These include:

- The Medtronic Cardioblate® System (Medtronic, Minneapolis, MN; cleared for marketing in January 2002);
- The Cardima Ablation System (Cardima, San Carlos, CA; cleared for marketing in January 2003);
- The Epicor™ Medical Ablation System (Epicor Medical, Sunnyvale, CA; cleared for marketing in February 2004);
- The Isolator™ Transpolar™ Pen (AtriCure, West Chester, OH; cleared for marketing in June 2005);
- The Estech COBRA® Cardiac Electrosurgical Unit (Endoscopic Technologies, Danville, CA; cleared for marketing in December 2005);
- The Coolrail™ Linear Pen (AtriCure, West Chester, OH; cleared for marketing in March 2008);
- The Numeris® Guided Coagulation System with VisiTrax® (nContact Surgical, Morrisville, NC; cleared for marketing in November 2012).

A number of cryoablation systems which may be used on cardiac ablation procedures have also been cleared for marketing, including:

- The Cryocare® Cardiac Surgery System (Endocare, Irvine, CA; cleared for marketing in March 2002);
- The SeedNet™ System (Galil Medical; cleared for marketing in May 2005);
- SurgiFrost® XL Surgical CryoAblation System (CryoCath Technologies, Kirkland, Quebec, acquired by Medtronic; cleared for marketing in July 2006);
- The Isis™ cryosurgical unit (Galil Medical; cleared for marketing in March 2007)

FDA Product Code: OCL.

**Related Policies**

2.02.19 Catheter Ablation as Treatment for Atrial Fibrillation
2.02.01 Catheter Ablation of Cardiac Arrhythmias
2.02.26 Percutaneous Left Atrial Appendage Closure Devices for Stroke Prevention in Atrial Fibrillation
Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

The maze or modified maze procedure, performed on a non-beating heart during cardiopulmonary bypass with concomitant cardiac surgery is considered medically necessary for treatment of symptomatic, drug-resistant atrial fibrillation or flutter.

Minimally invasive, off-pump maze procedures (ie, modified maze procedures), including those done via mini-thoracotomy, are considered not medically necessary for treatment of atrial fibrillation or flutter.

Hybrid ablation (defined as a combined percutaneous and thoracoscopic approach) is considered not medically necessary for the treatment of atrial fibrillation or flutter.

The use of an open maze or modified maze procedure performed on a non‒beating heart during cardiopulmonary bypass without concomitant cardiac surgery is considered not medically necessary for treatment of symptomatic, drug-resistant atrial fibrillation or flutter.

Policy Guidelines

Given the availability of less-invasive alternative approaches in the treatment of atrial fibrillation (AF; see policy 2.02.19), performing the maze procedure without concomitant cardiac surgery should rarely be needed.

Published studies on the maze procedure describe patients with drug-resistant AF and atrial flutter as having experienced their arrhythmias for an average of 7 or more years and having unsuccessful results with an average of 5 or more antiarrhythmic medications.

Rationale

The policy is based on a 1994 TEC Assessment. (1)

Traditional Maze vs “Modified Maze” procedures

Khargi et al analyzed 48 studies comprising 3832 patients who received surgical treatment of atrial fibrillation (AF) using the classic “cut and sew” Cox-Maze III technique or an alternative source of energy. (2) They concluded that they could not identify any significant differences in the postoperative sinus rhythm conversion rates between the classical approach and alternative sources of energy. While prospective randomized studies are lacking, the data involve a wide range of ablative patterns and their effects on atrial tissue. Topkara et al reported comparable postoperative rhythm success in use of
either radiofrequency (RF, 121 patients) or microwave (85 patients) energy in surgical ablation of atrial fibrillation. (3)

Several observational studies compared the Cox-Maze III procedure with other procedures (RF ablation, pulmonary vein isolation) performed at single institutions, with procedure selection guided by the surgeon. Two studies attempted to address the selection bias inherent in these studies by matching. In the first, from the Washington University School of Medicine, wherein the maze procedure was developed, the 242 patients who underwent the Cox-Maze procedure (154 with the classic cut and sew [CMIII] procedure, and 88 in whom RF ablation replaced the incisions of the classic procedure [CMIV]) were matched on their propensity for treatment assignment (a logistic regression in which the outcome is treatment assignment and the predictors are covariates that might influence which procedure is chosen by the surgeon). (4) Fifty-eight matched pairs were studied. At 1 year, survival was 94% and 89% (p=0.19) and freedom from AF recurrence was 96% and 93% (p=0.52) for the CMIII and CMIV groups, respectively. The authors note that the CMIV procedure was offered to higher risk patients than the CMIII procedure, which is partly why only 58 of 88 CMIV patients were able to be matched in their analysis. The matched propensity analysis is able to remove measureable selection biases, but if unmeasured factors lead surgeons to choose one surgery over the other, these factors are not accounted for in the analysis.

In a second matched analysis, 56 patients who underwent a CMIV RFA procedure at Mayo Clinic were matched (historical controls) to 56 patients who underwent the CMIII procedure. (5) Matching factors were age, sex, New York Heart Association (NYHA) class, AF type, and concomitant mitral valve surgery. Here the CMIV group had greater postoperative AF (43% vs 24%), more pacemaker requirements (25% vs 5%), more antiarrhythmic drug use (75% vs 25%), and fewer patients with freedom from AF at late follow-up (mean 8.4 months) (62% vs 92%). Again, the CMIV patients had greater underlying disease (more concomitant procedures were performed).

In a second article reporting results from the Mayo Clinic, Stulak et al reported results from an unmatched retrospective comparison of CMIII and CMIV among 1540 patients who underwent surgical ablation for AF at a single institution from 1993 to 2011. (6) Energy sources included cut and sew in 521 (44%), cryothermy in 267 (22%), RF in 262 (22%), and a combination in 139 patients (12%). On multivariate analysis, CMIII was independently associated with less risk of recurrent AF at a follow-up period of 1 to 5 years (hazard ratio [HR], 0.4; 95% confidence interval [CI], 0.24 to 0.69; p<0.001) and more than 5 years (HR=0.23; 95% CI, 0.12 to 0.42; p<0.001) for all patients. This study is limited by its retrospective design and lack of propensity score matching.

Section Summary Traditional Maze Versus “Modified Maze” Procedures
There are numerous modifications on the original maze procedure, with variations in the surgical approach, the lesion set used, and the methods for creating lesions (eg, cut and sew, RFA). The evidence on comparative effectiveness of the different approaches is not of high quality, and is incomplete in terms of addressing all of the possible comparisons. The limited available evidence from matched case series does not indicate that there are large differences in efficacy among the different approaches.
Maze and Related Procedures as an Adjunct to Open Heart Surgery

The evidence on this question consists of several RCTs evaluating AF ablation when performed as an add-on for patients undergoing open mitral valve surgery, and systematic reviews of these trials.

Systematic Reviews
In 2014, Phan et al reported results of a systematic review and meta-analysis of RCTs comparing surgical ablation with no ablation among patients with AF undergoing mitral valve surgery. (7) Nine studies were included in the analysis, 4 that evaluated RFA, 1 that evaluated RFA with port access, 3 that evaluated Cox-Maze cut-and-sew, 1 that evaluated cryoablation, and 1 that evaluated pulmonary vein isolation. In pooled analysis, the risk of 30-day all-cause mortality did not differ significantly between the mitral valve repair plus AF ablation (AFA) and the mitral valve repair only groups (4.4% vs 2.7%, respectively; odds ratio [OR], 1.45; 95% CI, 0.55 to 3.83; p=0.46). The number of patients in sinus rhythm at discharge was significantly higher in the mitral valve repair plus AF ablation group compared with the mitral valve repair only group (67.9% vs 17.0%; OR=13.96; 95% CI, 6.29 to 30.99; p<0.001); similarly, at 3-, 6-, 12-, and greater than 12-month follow-ups, a greater proportion of the mitral valve repair plus AFA was in sinus rhythm.

In an earlier systematic review, Reston et al reviewed 4 randomized controlled trials (RCTs) and 6 comparative studies to determine whether a simultaneous maze procedure reduces the risk of stroke or death in patients with chronic or paroxysmal atrial fibrillation (AF) who receive mitral valve surgery. (8) They concluded that the studies support a reduction in stroke rates and a small increased risk in need for pacemakers among patients receiving simultaneous maze procedures. The authors also conclude that alternative energy sources, such as RF, may reduce the risk of postoperative bleeding associated with classic maze incisions.

Randomized controlled trials (RCTs)
Several additional RCTs evaluating AFA in conjunction with open surgery that were not included in the systematic reviews have been published. In 2015, Gillinov et al published results of a large RCT that randomized 260 patients with persistent or long-standing AF who required mitral valve surgery to either ablation (either pulmonary vein isolation or ablation with a maze lesion set) during surgery (n=133) or no ablation (n=127). (9) Compared with controls, significantly more patients in the ablation group were free from AF at both 6 months and 12 months (63.2% vs 29.4%, p<0.001). The relative success ratio (ablation group:control group) was 2.15 (95% CI, 1.54 to 3.00) of observed data. At 1 year, mortality did not differ significantly between the ablation group and the control group (6.8% vs 8.7%, respectively, p=0.57). Serious adverse event rates did not differ significantly between groups at 30 days or 1 year.

Budera et al published an RCT in 2012, which randomized 224 patients from 3 clinical centers to cardiac surgery plus ablation versus cardiac surgery alone. (10) Patients were eligible for inclusion if they had at least 2 episodes of documented AF in the last 6 months, as well as appropriate indications for cardiac surgery. Cardiac surgery procedures included coronary artery bypass graft (CABG), valve replacement/repair, or combined CABG and valve procedures. The primary efficacy outcome was sinus
rhythm at one year following surgery, and the primary safety outcome was a composite outcome of death, myocardial infarction, stroke, or new-onset renal failure requiring hemodialysis at 30 days following surgery. Sinus rhythm at 1 year was documented in 60.2% (56/93) of patients in the surgery plus ablation group compared with 35.5% (27/76) patients in the surgery-alone group. Adverse events were similar in both groups at 30 days and at one-year follow-up. Secondary clinical outcomes, included mortality and NYHA functional class, did not differ between groups at one year.

The SAFIR study (11) was a multicenter, double-blind, RCT conducted at 4 university hospitals. This trial randomly assigned 43 patients with mitral valve disease and long-standing persistent AF to mitral surgery alone versus surgery plus RFA of the left atrium. At 12 months, 95% of patients in the RFA were in sinus rhythm compared with 33.3% of patients in the surgery-alone group (p<0.005). The primary endpoint of sinus rhythm at 12 months without recurrence of any atrial arrhythmias was reached by a significantly greater percent of patients in the RFA group (57% vs. 4%, respectively; p=0.004). Rates of postoperative complications and stroke were similar between groups.

Von Oppell et al. (12) randomly assigned 49 patients with AF of greater than 6 months who were scheduled for mitral valve surgery to a modified RF maze procedure versus valve surgery alone. At 12 months of follow-up, more patients in the maze group remained in sinus rhythm (75% vs. 39%, respectively; p=0.03). There was also a significant decrease in amiodarone use for the maze group and no difference in the use of warfarin.

Liu et al (13) compared mitral valve surgery plus a modified maze procedure to mitral valve surgery alone followed by RF catheter ablation 6 months later in 99 patients with rheumatic heart disease. After a mean follow-up of 15 to 20 months, patients in the maze group had a higher rate of freedom from atrial arrhythmias compared to the RFA group (82% vs. 55.2%, respectively; p<0.001). Repeat procedures were required for 15/50 patients in the RFA group. Percutaneous catheter ablation was performed in 6/49 patients in the maze group for recurrent arrhythmias.

Van Breugel et al (14) evaluated changes in quality of life (QOL) in a related patient population. One-hundred fifty patients with AF who were scheduled to undergo either valve surgery or CABG surgery were randomly assigned to surgery alone versus surgery plus a modified maze procedure. The primary endpoint was QOL as measured by the 36-Item Short-Form Health Survey, the EuroQoL (eQ)-5D, and the Multidimensional Fatigue Inventory. A total of 132 patients had usable survey results. Both groups improved on all QOL measures, but in general there were no significant differences between groups. The only exception was on the pain/discomfort subscale of the eQ-D, which showed a greater degree of worsening in the control group compared to the maze group.

In another evaluation of QOL, Chernyavskiy et al reported that randomized to CABG with a modified maze procedure (n=30) or with pulmonary vein isolation by radiofrequency ablation (n=31) had improved QOL scores compared with those randomized to CABG alone (n=34). (15)

Nonrandomized Comparative Studies
Saint et al attempted to quantify the incremental risk conferred by adding a Cox-Maze IV procedure to open mitral repair in a comparison of 213 patients with mitral valve disease and preoperative AF who underwent mitral valve surgery only (n=109) or mitral valve surgery with a Cox-Maze IV procedure (n=104).(16) The operative mortality for the mitral valve procedure alone was predicted for each group based on Society of Thoracic Surgeons (STS) perioperative risk calculator; the risk attributed to the Cox-Maze IV procedure addition was calculated by comparing the predicted mortality from the isolated mitral valve procedure with the actual mortality rate. At baseline, patients who had an isolated mitral valve procedure differed significantly from those who underwent the mitral valve procedure plus a Cox-Maze IV procedure in terms of medical comorbidities and etiology of the mitral valve disease. The observed 30-day mortality for patients not offered a Cox-Maze IV procedure was 4.6% (expected 5.5%), yielding an observed: expected 30-day mortality ratio of 0.84 (95% CI, 0.13 to 1.54). The observed 30-day mortality for patients who underwent a concomitant Cox-Maze IV procedure with mitral valve surgery was 2.9%. The STS predicted score for isolated mitral valve surgery in this group was 2.5%, yielding an observed: expected 30-day mortality ratio of 1.16 (95% CI, 0.13 to 2.44). This study is limited by the fact that patients who received concomitant Cox-Maze IV procedures with mitral valve surgery were a selected low-risk population; however, it suggests that in the appropriate patient population, the Cox-Maze IV can be added on to mitral surgery with limited additional short-term mortality risk.

Noncomparative Studies
Since the publication of the RCTs previously described, several noncomparative studies have reported outcomes from surgical (“cut-and-sew”) maze and modified RF maze procedures as an adjunct to planned cardiac surgery. While single-arm studies can offer useful data on some parameters, such as durability of treatment effect and adverse events, they do not offer relevant evidence on the comparative efficacy of the procedure. For example, a study of long-term outcomes after 127 Cox-Maze cut-and-sew procedures in conjunction with mitral valve replacement was identified. (17) Patient disposition was well-documented in the analysis. Thirty percent of patients experienced late AF recurrence at a mean of 44±27 months. Freedom from AF was 93%, 82%, 71%, and 63% at 1, 3, 5, and 7 years, respectively, and pacemakers were implanted in 4.7% of patients. Other case series have reported success rates of the procedure in different populations, with rates of freedom from AF ranging from 53% to 79% at latest follow-up. (18-20)

Section Summary: Maze and Related Procedures as an Adjunct to Open Heart Surgery
Surgical treatment of AF can be performed in conjunction with valvular surgery or CABG surgery with little additional risk. Evidence from RCTs of open heart surgery plus surgical treatment of AF versus surgery alone establishes that there is a high rate of success in maintaining sinus rhythm and avoiding the need for antiarrhythmic medications. Evidence for a benefit in other health outcomes, such as stroke rate or quality of life, is currently insufficient to form conclusions.

Maze and Related Procedures as a Stand-Alone Treatment for AF
The evidence related to the use of maze and related procedures as standalone treatments for AF includes evaluations of open surgical ablation, minimally invasive surgical ablation, and “hybrid” approaches. The stand-alone procedures fall on a continuum of invasiveness, ranging from open repair with sternotomy to minimally invasive procedures done with video-assisted thoracoscopy. Hybrid
approaches include concomitant epicardial/endocardial procedures and are discussed separately. The optimal study design for evaluating the effectiveness of these procedures is an RCT that includes clinically relevant measures of health outcomes. Intermediate outcome measures, also known as surrogate outcome measures, may also be adequate if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies can sometimes provide useful information on health outcomes, but may be affected by biases due to multiple confounding factors. Uncontrolled studies may provide useful information on procedure-related harms, but do not, by themselves, provide relevant information on the comparative efficacy of treatments. For Maze and related procedures as stand-alone therapy, the appropriate comparison group is endocardial catheter ablation. Although freedom from AF is an important outcome following AF treatment procedures, the evaluation of stand-alone maze and related procedures requires assessment of surgery-related complications.

Surgical Ablation as a Stand-Alone Treatment

Randomized Controlled Trials

One RCT has been completed that compares stand-alone surgical ablation versus percutaneous ablation. (21) The FAST trial enrolled 124 patients, from 2 clinical centers in Europe, who had symptomatic AF for at least 1 year and had failed at least 1 antiarrhythmic medication. Patients were randomized to surgical ablation using video-assisted thoracoscopic surgery under general anesthesia, or to percutaneous catheter ablation. Both techniques used RF energy. All patients in the surgical group also had surgical removal of the left atrial appendage. The primary outcome was freedom from AF off all antiarrhythmic medications during 12 months of follow-up. Secondary outcomes were freedom from AF including patients on medications, and adverse events. Prior unsuccessful catheter ablation had been performed in 67% of patients.

At 1 year, freedom from AF off all antiarrhythmic drugs was achieved by 65.6% (40/61) of the surgical patients compared to 36.5% (23/63) of the catheter ablation patients (p=0.002). Freedom from AF, on or off medications, was achieved by 78.7% (48/61) in the surgical group compared to 42.9% (27/63) in the catheter ablation group (p<0.001). Serious adverse events were more common in the surgical group, occurring in 23.0% (14/61) of patients compared with 3.2% (2/63) in the catheter ablation group (p=0.001). In both groups, there was 1 episode each of tamponade and stroke. Additional complications in the surgical group were 6 patients who had pneumothorax, 2 patients who required pacemaker insertion, and 1 patient each who had hemotherax, rib fracture, pneumonia, or required sternotomy for bleeding. In the catheter ablation group, 6.3% (4/63) of patients had a groin hematoma, which was considered a minor complication.

In a subsequent smaller RCT, Pokushalov et al randomized patients with a prior failed first catheter ablation procedure for AF to receive either repeat catheter ablation (n=32) or surgical ablation with video-assisted thoracoscopic surgery (n=32). (22) After 12 months, a higher proportion of patients who underwent surgical ablation were free of AF or atrial tachycardia without antiarrhythmic drugs (81% vs 47%, p=0.004). Although the total number of adverse events did not differ significantly between groups, the number of serious adverse events was higher in the surgical ablation group (7 vs 1, p=0.02).
Systematic Reviews

A number of systematic reviews that have used different inclusion criteria have summarized the evidence on stand-alone surgical ablation. These studies have varied in their inclusion criteria. In 2015, Phan et al reported results of a systematic review and meta-analysis of studies comparing thoracoscopic surgical ablation with catheter ablation, including the FAST trial. (23) Eight comparative studies, with a total of 321 VATS ablation patients and 378 catheter ablation patients, met the inclusion criteria. For the study’s primary efficacy end point of freedom of AF off antiarrhythmic drugs, the treatment success was significantly higher in the surgical ablation group compared with the catheter ablation group at 6 months postprocedure (81% vs 64.3%; risk ratio [RR], 1.23; 95% CI, 1.02 to 1.49; p=0.03). This difference was maintained at 12 months postprocedure. Surgical ablation-treated patients had higher rates of major complications (including death, stroke, transient ischemic attack, pericardial effusion, cardiac tamponade, pulmonary vein stenosis, pneumothorax, hemothorax, pneumonia, myocardial infarction, conversion to complete thoracotomy), compared with catheter ablation-treated patients (28.2% vs 7.8%; RR=3.30; 95% CI, 1.73 to 6.29; p<0.001).

A systematic review of 28 single-arm studies reporting on 1051 patients who received minimally invasive surgical treatment for AF was published in 2012 by La Meir et al. (24) This review noted substantial differences in patient population, surgical techniques, and definitions of outcome across studies. At 1 year, the range of success, as defined by freedom from AF and off all medications, was 51% to 86%. Outcomes for RFA appeared superior to those using ultrasound or microwave energy sources. The authors also noted that success was higher for the population of paroxysmal AF compared with persistent and permanent. The early complication rate ranged from 0% to 39%, and the most common major complications were conversion to sternotomy, bleeding, port access problems, cardiac events, cerebrovascular accidents, and pulmonary complications.

A similar systematic review of 23 case series using minimally invasive surgical treatment for AF was published in 2013 by Krul et al. (25) Surgical techniques varied considerably among the included studies. At 1-year follow-up, the combined estimate for single-procedure success rates off all antiarrhythmic drugs was 69% (95% CI, 58% to 78%), and for patients still taking antiarrhythmic drugs, the rate was 79% (95% CI, 71% to 85%). Mortality occurred in 0.4% of patients, and complications were reported in 12.8% of patients.

Non-randomized Comparative Studies

There are several observational studies that include a matched comparison group of patients who receive alternate treatments. These case series with matched control groups offer stronger evidence for comparative efficacy than do single-arm case series. Stulak et al (26) compared 97 patients who underwent an isolated cut-and-sew Cox-Maze procedure with 194 patients who underwent catheter ablation for AF. Cox-Maze patients were matched according to age, sex, and AF type on a 1:2 basis with patients undergoing catheter ablation. At last follow-up 82% of patients who underwent the Cox-Maze were free of AF off all meds compared to 55% of patients who underwent catheter ablation (p<0.001). By life table analysis, freedom from AF at 5 years was estimated to be 87% following Cox-Maze compared to 28% following catheter ablation (p<0.001).
Wang et al (27) performed a retrospective matched comparison of 83 patients who underwent minimally invasive surgical ablation with 83 patients who underwent catheter ablation. All patients had long-standing persistent AF, were treated between 2006 and 2009 and followed ranged from 1 to 3.6 years. At last follow-up, 74.7% of patients who underwent surgical ablation were free of AF compared with 59.0% of the patients treated with catheter ablation (p<0.05). Freedom from AF off all drugs was 61.4% in the surgical group compared to 44.6% in the catheter ablation group (p<0.05).

Other observational studies report outcomes for stand-alone AF treatment. Representative studies are described next.

Lawrance et al conducted a retrospective cohort study comparing patients who underwent a Cox-Maze IV procedure either by right minithoracotomy (n=104) or sternotomy (n=252) at a single center from 2002 to 2014. (28) Patients included in the series could also have undergone a concomitant mitral valve procedure, if indicated. Freedom from atrial tachyarrhythmias off antiarrhythmic drugs was not significantly different between groups. The overall complication rate was lower in the minithoracotomy group and the sternotomy group (6% vs 13%, p=0.044).

De Maat et al published results of a retrospective observational study of minimally invasive surgical treatment for AF in 86 patients with symptomatic, drug-refractory paroxysmal or permanent AF. (29) Patients were treated by at 3 centers, via bilateral video-assisted mini-thoracotomy from 2005 to 2007 (n=13 patients) and subsequently via a totally thoracoscopic approach from 2007 to 2011 (n=73 patients). Fifteen patients (17%) had previous transcatheter ablation performed. The percentage of the patients free from atrial arrhythmias without the use of antiarrhythmic drugs was 71% at 12 months, 72% at 24 months, and 69% at 36 months. Half of the 24 treatment failures underwent an additional transcatheter ablation. Major periprocedural adverse events occurred in 8%, which included 3 requirements for sternotomy or mini-thoracotomy due to complications, 2 cases of late pericardial tamponade, and 1 pericardial effusion requiring video-assisted thoracoscopic surgery, and 1 stroke.

Massimiano et al reported outcomes for 292 consecutive patients from a single institution who underwent minimally invasive mitral valve surgery (n=177), surgical ablation for AF (n=81), or both (n=34). (30) Among the 115 patients who underwent AF ablation, the percentage of patients in sinus rhythm at 6, 12, and 24 months was 93%, 93%, and 88%, respectively; the percentage of patients in sinus rhythm and not taking class I and III antiarrhythmic medications at 6, 12, and 24 months was 85%, 85%, and 77%, respectively.

**Single-Arm Studies**

Numerous single-arm case series report high success rates following one of these surgical procedures; however, these case series offer limited evidence regarding the efficacy of the procedure itself. (31-40) Most of the case series are limited by a lack of control group, generally only report short-term outcomes, and do not consistently report adverse events.
Several single-arm case series of minimally invasive epicardial ablation report on the population of patients who had failed catheter ablation. These case series offer evidence that is more clinically relevant than studies of unselected patients, because this population has more limited treatment options and is more likely to benefit from surgical procedures. However, these studies only offer very limited evidence about comparative efficacy with alternatives such as catheter ablation. Ad et al (41) reported on 40 patients who had failed catheter ablation, with a mean of 2.3 prior ablations per patient. Maintenance of sinus rhythm at 6, 12, and 24 months was 76% (29/38), 89% (23/26), and 93% (13/14), respectively. Castella et al (40) enrolled 34 patients who had failed a mean of 2.0 prior catheter ablations; 17 with paroxysmal AF, 12 with persistent AF, and 5 with long-standing persistent AF. At 1-year follow-up sinus rhythm was maintained in 82% of patients with paroxysmal AF, 60% with persistent AF, and 20% with long-standing persistent AF.

Hybrid Procedures as Stand-Alone Treatment
The evidence on hybrid ablation consists of a number of case series, one of which included a matched comparison group of patients undergoing percutaneous ablation. The study with a comparison group enrolled 35 patients who underwent a hybrid procedure and 28 patients who underwent a standard percutaneous procedure. (43) Approximately two-thirds of the patients (42/63) had undergone a previous percutaneous ablation procedure. At 1 year, there were more patients in the hybrid group who were free of AF, but this difference did not reach statistical significance (91.4% vs. 82.1%, p=0.07). On subgroup analysis, the success rate was higher for the hybrid group in patients with long-standing persistent AF (81.8% vs 44.4%; p=0.001). More patients in the hybrid group were on warfarin at one year (29% vs. 13.4%, p<0.001). There was no difference between groups on the frequency of adverse events.

Other single-arm case series have been published that include populations of 19-101 patients. (44-53). These series consistently report high success rates in maintaining sinus rhythm at one-year follow-up, ranging from 71-91%. Some of these series report individual adverse events, but reporting on adverse events is variable and not systematic in these case series, resulting in an inability to accurately estimate rates of adverse events.

Je et al reported results of a systematic review of 37 studies designed to compare minimally invasive AF ablation procedures, including minimally invasive endocardial Cox-Maze procedure with cardiopulmonary bypass support, epicardial surgical ablation, and hybrid surgical ablation. (54) The studies included were 2 studies on minimally invasive endocardial Cox-Maze procedure (total sample size, 145 patients), 26 on epicardial surgical ablation (1382 patients), and 9 on hybrid surgical ablation (350 patients). No statistical analyses or meta-analyses were possible due to the heterogeneity in methodology and data reporting. However, the authors do report that treatment success (sinus rhythm without antiarrhythmic medications) at 12 months was 87% for the endocardial Cox-Maze procedure, 72% for epicardial surgical ablation, and 71% for hybrid surgical ablation.

Section Summary: Maze and Related Procedures as a Stand-Alone Treatment for AF
The evidence on the role of maze and related procedures as stand-alone procedures consists of 2 RCTs (FAST study) and many case series, some with matched control groups. The RCTs report higher
success at maintaining sinus rhythm at 1 year of follow-up with thoracoscopic ablation, but also report higher adverse event rates compared with catheter ablation. This evidence does not clearly support the superiority of 1 technique over the other, but suggests that other factors such as type of AF, prior treatments, inability to take anticoagulation, and patient preference may influence the decision for type of procedure. Case series with matched control groups also report higher success in maintaining sinus rhythm compared with catheter ablation. The single-arm case series corroborate the high success rates following surgical treatment, but do not provide sufficient evidence to form conclusions on the comparative efficacy of surgical treatment versus other treatments.

Some case-series and one of the RCTs include only patients who have failed previous catheter ablation. These studies also report high success rates following thoracoscopic ablation, suggesting that patients who fail catheter ablation may still benefit from thoracoscopic ablation. However, the RCT demonstrated higher adverse event rates compared with catheter ablation, and the risk-benefit ratio is not well defined.

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>
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<tbody>
<tr>
<td>Ongoing</td>
<td></td>
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<tr>
<td>NCT00703157a</td>
<td>The SCALAF Success Trial</td>
<td>80</td>
<td>Apr 2016</td>
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<tr>
<td>NCT02047279</td>
<td>Left Atrium Reduction Versus no Left Atrium Reduction for Patients</td>
<td>100</td>
<td>Dec 2017</td>
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<tr>
<td></td>
<td>With Enlarged Left Atria and Persistent or Long Standing Persistent</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atrial Fibrillation Undergoing Mitral Valve Surgery</td>
<td></td>
<td></td>
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<tr>
<td>Unpublished</td>
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<tr>
<td>NCT01319747a</td>
<td>Video-Assisted Thoracoscopic Pulmonary Vein Isolation Versus</td>
<td>160</td>
<td>Feb 2013</td>
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<tr>
<td></td>
<td>Percutaneous Catheter Ablation in Atrial Fibrillation Trial</td>
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<td>(unknown)</td>
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<tr>
<td>NCT01442181</td>
<td>Minimally Invasive Surgical Treatment Versus Medical Management</td>
<td>30</td>
<td>Nov 2014</td>
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<tr>
<td></td>
<td>for Stroke Patients With Atrial Fibrillation</td>
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<td>(has results)</td>
</tr>
<tr>
<td>NCT01582828</td>
<td>Serial Hybrid Atrial Fibrillation Ablation</td>
<td>162</td>
<td>Dec 2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(unknown)</td>
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<tr>
<td>NCT01891825</td>
<td>Persistent Atrial Fibrillation Ablation Trial</td>
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<td>Sep 2016</td>
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<tr>
<td></td>
<td></td>
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<td>(suspended)</td>
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NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial

Practice Guidelines and Position Statements

In 2014, the American Heart Association, American College of Cardiologists, and the Heart Rhythm Society (HRS) issued guidelines on the management of patients with AF. (55) The guideline provides the following recommendations related to the use of surgical ablation to maintain sinus rhythm:

- Class IIa recommendations: An AF surgical ablation procedure is reasonable for selected patients with AF undergoing cardiac surgery for other indications. (Level of Evidence: C)
• Class IIb recommendations: A stand-alone AF surgical ablation procedure may be reasonable for selected patients with highly symptomatic AF not well managed with other approaches. (Level of Evidence: B)

A 2012 expert consensus statement was developed by the HRS, the European Heart Rhythm Association, European Cardiac Arrhythmia Society. The document was also endorsed by the American College of Cardiology, the American Heart Association, the Asia Pacific Heart Rhythm Society, and the Society of Thoracic Surgeons. (56)

The following recommendations were made regarding concomitant surgical ablation in patients undergoing cardiac surgery for other purposes and who have symptomatic AF:

• Paroxysmal: Surgical ablation is reasonable for patients undergoing surgery for other indications (IIa recommendations, level of evidence C)
• Persistent: Surgical ablation is reasonable for patients undergoing surgery for other indications (IIa recommendations, level of evidence C)
• Longstanding Persistent: Surgical ablation is reasonable for patients undergoing surgery for other indications (IIa recommendation, level of evidence C)

The following recommendations were made regarding stand-alone surgical ablation in patients with symptomatic AF refractory or intolerant to at least on Class 1 or 3 antiarrhythmic medication:

• Paroxysmal: Stand-alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach (IIb recommendation, level of evidence C)
• Paroxysmal: Stand-alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation (IIb recommendation, level of evidence C)
• Persistent: Stand-alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach (IIb recommendation, level of evidence C)
• Persistent: Stand-alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation (IIb recommendation, level of evidence C)
• Longstanding Persistent: Stand-alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach (IIb recommendation, level of evidence C)
• Longstanding Persistent: Stand-alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation (IIb recommendation, level of evidence C)

The following recommendations were made regarding stand-alone surgical ablation in patients with symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent:

• Paroxysmal: Stand-alone surgical ablation is not recommended (III recommendation, level of evidence C)
Persistent: Stand-alone surgical ablation is not recommended (III recommendation, level of evidence C)

Longstanding Persistent: Stand-alone surgical ablation is not recommended (III recommendation, level of evidence C)

The Canadian Cardiovascular Society published guidelines in 2010 on surgical therapy for atrial fibrillation. (57) These guidelines state that there is a high rate of freedom from AF following surgical treatment, 70% to 85% at 1 year, but that surgical ablation of AF has not been shown to alter mortality. The following recommendations were made:

“We recommend that a surgical AF ablation procedure be undertaken in association with mitral valve surgery in patients with AF when there is a strong desire to maintain sinus rhythm, the likelihood of success of the procedure is deemed to be high, and the additional risk is low (Strong Recommendation, Moderate-Quality Evidence).

We recommend that patients with asymptomatic lone AF, in whom AF is not expected to affect cardiac outcome, should not be considered for surgical therapy for AF (Strong Recommendation, Low-Quality Evidence).

In patients with AF who are undergoing aortic valve surgery or coronary artery bypass surgery, we suggest that a surgical AF ablation procedure be undertaken when there is a strong desire to maintain sinus rhythm, the success of the procedure is deemed to be high, and the additional risk low (Conditional Recommendation, Low-Quality Evidence). This recommendation recognizes that left atrial endocardial access is not routinely required for aortic or coronary surgery.

We recommend that oral anticoagulant therapy be continued following surgical AF ablation in patients with a CHADS2 score ≥2 (Strong Recommendation, Moderate-Quality Evidence).”

Although not a formal recommendation, this guideline stated that stand-alone surgical ablation should be considered after failure of prior attempts at catheter ablation and antiarrhythmic drugs.

CVS published a 2012 focused update to their comprehensive 2010 guidelines on AF. (58) The 2012 focused guidelines discuss the use of anticoagulants in the treatment of AF.

U.S. Preventive Services Task Force Recommendations
Not applicable

Summary of Evidence
For individuals who have symptomatic, drug-resistant atrial fibrillation (AF) or flutter who are undergoing cardiac surgery with bypass who received a Cox maze procedure or modified maze procedure, the
evidence includes several randomized controlled trials (RCTs) and nonrandomized comparative studies, along with systematic reviews of these studies. Relevant outcomes are overall survival, medication use, and treatment-related morbidity. The most direct evidence comes from several small RCTs confirm the benefit of a modified maze procedure for patients with AF who are undergoing mitral valve surgery. These trials establish that the addition of a modified maze procedure results in a lower incidence of atrial arrhythmias following surgery, with minimal additional risks. Observational studies support the RCT findings. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have symptomatic, drug-resistant AF or flutter who are not undergoing cardiac surgery with bypass who receive minimally invasive, off-pump thoracoscopic maze procedures, the evidence includes RCTs and observational studies, some of which identify control groups. Relevant outcomes are overall survival, medication use, and treatment-related morbidity. The most direct evidence comes from 1 RCT comparing surgical AF ablation with video-assisted thoracoscopy with percutaneous catheter ablation, which reported higher success at maintaining sinus rhythm at 1 year of follow-up with thoracoscopic ablation, but also reported higher adverse event rates compared with catheter ablation. The case series generally report high success rates, and the few case series with matched comparison groups report higher success rates with surgical treatment compared with catheter ablation. However, this evidence does not permit definitive conclusions whether 1 approach is superior to the other. Factors such as previous treatment, the probability of maintaining sinus rhythm, the risk of complications, contraindications to anticoagulation, and patient preference may all affect the risk-benefit ratio for each procedure. At present, it is not possible to define a subgroup of patients who will benefit more from thoracoscopic (or other minimally invasive) surgical ablation compared with percutaneous ablation, so the risks and benefits of surgical ablation compared with catheter ablation are not well-defined. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have symptomatic, drug-resistant AF or flutter who are not undergoing cardiac surgery with bypass who receive hybrid thoracoscopic/endocardial ablation procedures, the evidence includes 1 nonrandomized comparative study and single-arm case series. Relevant outcomes are overall survival, medication use, and treatment-related morbidity. The studies suggest that hybrid ablation procedures are associated with high rates of freedom from AF, but direct comparisons with catheter ablation are lacking. Comparative studies are needed allow direct comparisons of the benefits and harms of hybrid ablation procedures compared with alternatives. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Medicare National Coverage**

There is no national coverage determination (NCD).

**References**


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<th>Section: Surgery</th>
<th>Effective Date: October 15, 2016</th>
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<tr>
<td>Subsection: Surgery</td>
<td>Original Policy Date: September 14, 2012</td>
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<tr>
<td>Subject: Open and Thoracoscopic Approaches to Treat Atrial Fibrillation and Atrial Flutter (Maze and Related Procedures)</td>
<td>Page: 19 of 21</td>
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**Policy History**

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<th>Action</th>
<th>Reason</th>
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<tr>
<td>March 2015</td>
<td>Update Policy</td>
<td>Policy updated with literature review; references 9, 21-22, 27, and 50-52 added. The phrase “without concomitant cardiac surgery” was removed from the medical necessary statement for maze or modified maze during cardiopulmonary bypass, with addition of “not medically necessary” statement for Maze done without concurrent cardiac surgery. “Atrial Flutter” added to title.</td>
</tr>
<tr>
<td>September 2015</td>
<td>Update Policy</td>
<td>Policy updated with literature review through March 29, 2016; references 15 and 40 added. Policy statements unchanged.</td>
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**Keywords**

Maze procedure
Modified Maze procedure

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 16, 2016 and is effective October 15, 2016.

Signature on file
Deborah M. Smith, MD, MPH