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

Policy Number: 7.01.14  Last Review: 8/2020
Origination: 1/2008  Next Review: 8/2021

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for the Maze procedure when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
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 atrial fibrillation or flutter.

When Policy Topic is not covered
Stand-alone minimally invasive, off-pump maze procedures (ie, modified maze procedures), including those done via mini-thoracotomy, are considered investigational for treatment of atrial fibrillation or flutter.

Hybrid ablation (defined as a combined percutaneous and thoracoscopic approach) is considered investigational 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 atrial fibrillation or flutter.

Considerations
Given the availability of less-invasive alternative approaches in the treatment of atrial fibrillation, 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.

### Description of Procedure or Service

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| **Individuals:**
  - With symptomatic atrial fibrillation or flutter who are undergoing cardiac surgery with bypass
| **Interventions of interest are:**
  - Cox maze or modified maze procedure
| **Comparators of interest are:**
  - Medical management
  - Catheter ablation
| **Relevant outcomes include:**
  - Overall survival
  - Medication use
  - Treatment-related morbidity |
| **Individuals:**
  - With symptomatic, drug-resistant atrial fibrillation or flutter not undergoing cardiac surgery with bypass
| **Interventions of interest are:**
  - Minimally invasive, off-pump thoracoscopic maze procedures
| **Comparators of interest are:**
  - Medical management
  - Catheter ablation
| **Relevant outcomes include:**
  - Overall survival
  - Medication use
  - Treatment-related morbidity |
| **Individuals:**
  - With symptomatic, drug-resistant atrial fibrillation or flutter not undergoing cardiac surgery with bypass
| **Interventions of interest are:**
  - Hybrid thoracoscopic and endocardial ablation procedures
| **Comparators of interest are:**
  - Medical management
  - Catheter ablation
| **Relevant outcomes include:**
  - Overall survival
  - Medication use
  - Treatment-related morbidity |

There are various 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 surgery. Surgical techniques have evolved to include minimally invasive approaches that use epicardial radiofrequency ablation, a thoracoscopic or mediastinal approach, and hybrid catheter ablations/open procedures.

For individuals who have symptomatic AF or flutter who are undergoing cardiac surgery with bypass who received a Cox maze or a 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. Several small RCTs have provided most of the direct evidence confirming the benefit of a modified maze procedure for patients with AF who are undergoing mitral valve surgery. These trials have established that the addition of a modified maze procedure results in a lower incidence of atrial arrhythmias following surgery, with minimal additional risks. Observational studies have supported these RCT findings. The evidence is sufficient to determine 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. Most of the direct evidence comparing surgical AF ablation with percutaneous catheter ablation comes from one RCT (FAST) that used video-assisted thoracoscopy in patients with antiarrhythmic drug-refractory atrial fibrillation with left atrial dilatation and hypertension, 67% of which had previously failed CA. In FAST, at one year, thoracoscopic ablation had higher success at maintaining sinus rhythm (36.5% for CA and 65.6% for surgical ablation), but also reported higher adverse event rates compared with CA. At 7 years, outcomes were consistently improved with thoracoscopic ablation, but interpretation of those findings is limited by important flaws in study conduct. In contrast, findings from a small single-center RCT in patients with no previous CA suggested no significant benefit with minimally invasive thoracoscopic ablation and more major complications. The case series have generally reported high success rates, and a few with matched comparison groups have reported higher success rates with surgical treatment than with catheter ablation. However, most series lacked a control group, generally only reported short-term outcomes, and did not consistently report adverse events. Therefore, this evidence does not permit definitive conclusions whether a specific 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. 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 and endocardial ablation procedures, the evidence includes a nonrandomized comparative study and single-arm case series. Relevant outcomes are overall survival, medication use, and treatment-related morbidity. The studies have suggested 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 to permit direct comparisons of the benefits and harms of hybrid ablation procedures with alternatives. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Background**

**Atrial Fibrillation**

AF is a supraventricular tachyarrhythmia characterized by disorganized atrial activation with ineffective atrial ejection. The underlying mechanism of AF involves the interplay between electrical triggering events that initiate AF 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 AF.

**Treatment**

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 and may also be used as first-line treatment. Catheter ablation is successful in maintaining sinus rhythm for most patients, but long-term recurrences are common and increase over time. Performed either by open surgical techniques or thoracoscopy, surgical ablation is an alternative approach to percutaneous catheter ablation.

**Open Surgical Techniques**
The classic Cox maze III procedure is a complex surgical procedure for patients with AF. It involves sequential atriotomy incisions that interrupt the aberrant atrial conduction pathways in the heart. 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 the surgical treatment of drug-resistant AF, with a success rate of approximately 90%.

The maze procedure entails making incisions in the heart that:

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

The classic Cox maze procedure is performed on a nonbeating 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 energy sources to create the atrial lesions instead of employing the incisional technique used in the classic maze procedure. The Cox maze IV procedure involves the use of radiofrequency energy or cryoablation to create transmural lesions analogous to the lesions created by the "cut-and-sew" maze.

**Minimally Invasive (Thoracoscopic) Techniques**
Less invasive, transthoracic, endoscopic, off-pump procedures to treat drug-resistant AF have been 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 thoracosscopic 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 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; radiofrequency energy is most commonly applied. Other energy sources such as cryoablation and high-intensity ultrasound have been used. For our purposes, the variations on surgical procedures for AF will be combined under the heading of "modified maze" procedures.

**Hybrid Techniques**

"Hybrid" ablation refers to the use of 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 a hybrid procedure is that a combination of both techniques may result in a complete ablation. Thoracoscopic epicardial ablation is limited by the inability to perform all possible ablation lines because 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 on separate days, as directed by the electrophysiology study.

**Regulatory Status**

Several radiofrequency ablation systems have been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process for cardiac tissue ablation (product code OCL). Table 1 provides a select list.

**Table 1. Radiofrequency Ablation Approved by the U.S. Food and Drug Administration**

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>510(k) Date</th>
<th>510(k) number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cobra Fusion Ablation System</td>
<td>AtriCure</td>
<td>Feb 2019</td>
<td>K190151</td>
</tr>
<tr>
<td>Medtronic Cardioblate® System</td>
<td>Medtronic</td>
<td>Jan 2002</td>
<td>K013392</td>
</tr>
<tr>
<td>Cardima Ablation System</td>
<td>Cardima</td>
<td>Jan 2003</td>
<td>K022008</td>
</tr>
<tr>
<td>Epicor™ Medical Ablation System</td>
<td>Epicor Medical</td>
<td>Feb 2004</td>
<td>K022894</td>
</tr>
<tr>
<td>Isolator™ Transpolar™ Pen</td>
<td>AtriCure</td>
<td>Jun 2005</td>
<td>K050459</td>
</tr>
<tr>
<td>Estech COBRA® Cardiac Electrosurgical Unit</td>
<td>Endoscopic Technologies</td>
<td>Jan 2006</td>
<td>K053326</td>
</tr>
</tbody>
</table>
A number of cryoablation systems, which may be used during cardiac ablation procedures, have also been cleared for marketing, including those in Table 2.

**Table 2. Cryoablation Systems Approved by the U.S. Food and Drug Administration**

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>510(k) Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryocare® Cardiac Surgery System</td>
<td>Endocare</td>
<td>Mar 2002</td>
</tr>
<tr>
<td>SeedNet™ System</td>
<td>Galil Medical</td>
<td>May 2005</td>
</tr>
<tr>
<td>SurgiFrost® XL Surgical CryoAblation System</td>
<td>CryoCath Technologies; now Medtronic</td>
<td>Jul 2006</td>
</tr>
<tr>
<td>Isis™ cryosurgical unit</td>
<td>Galil Medical</td>
<td>Mar 2007</td>
</tr>
</tbody>
</table>

**Rationale**

This evidence review was created in December 1995 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through March 16, 2020.

This review was informed by a TEC Assessment (1994).1

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function and include benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other
types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Maze and Related Procedures

Clinical Context and Therapy Purpose
The purpose of maze and related procedures in addition to on-bypass surgeries in patients who have AF is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does adding maze and related procedures to on-bypass surgeries improve the net health outcome in patients who have AF?

The following PICO was used to select literature to inform this review:

Patients
The relevant population of interest is individuals with symptomatic atrial fibrillation or flutter who are undergoing cardiac surgery with bypass

Interventions
The relevant interventions of interest are Cox maze or modified maze procedures added to on-bypass surgeries

Comparators
The relevant comparators of interest are medical management or catheter ablation

Outcomes
Relevant outcomes of interest are overall survival, medication use, and treatment-related morbidity

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Studies with duplicative or overlapping populations were excluded.

Traditional Maze vs "Modified Maze" Procedures

Review of Evidence
Systematic Reviews
Khargi et al (2005) analyzed 48 studies comprising 3832 patients who received surgical treatment for atrial fibrillation (AF) using the classic "cut-and-sew" Cox maze III technique or an alternative source of energy. Reviewers concluded they could not identify any significant differences in the postoperative sinus rhythm conversion rates between the classic approach and alternative sources of energy. While prospective randomized studies were lacking, the data involved a wide range of ablative patterns and their effects on atrial tissue. Topkara et al (2006) reported comparable postoperative rhythm success with both radiofrequency (RF; 121 patients) and microwave (85 patients) energy in surgical ablation of AF.

Randomized Controlled Trials
Subsequent to the systematic review described above, Zhang et al (2019) published results of a randomized controlled trial that randomized 120 patients who underwent valve surgery and bipolar radiofrequency ablation at a single hospital in West China. Patients were randomized to a left atrial maze IV procedure (LAM-IV) (n=60) or a modified LAM-IV (MLAM-IV) (n=60). In the MLAM-IV, rather than using a lesion set that passes over the left pulmonary veins (PVs), the anterior wall of the PV and the left atrial posterior wall (LAPW) are isolated as an entire box. At 5 years, there were no significant differences between the MLAM-IV and LAM-IV groups in the rate of freedom from AF (69.0% versus 60.0%; HR 0.71, 95% CI 0.39 to 1.32), late mortality (3.3% versus 6.0%; HR 0.5, 95% CI, 0.09 to 2.71), or cumulative major adverse events (16.7% versus 23.3%; HR 0.68, 95% CI, 0.30 to 1.52). However, a larger, multicenter RCT is still needed to confirm these findings.

Observational Studies
Several observational studies have compared the Cox maze III procedure with other procedures (radiofrequency ablation [RFA], 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 using matching. In the first, from a U.S. university medical school wherein the maze procedure was developed, Lall et al (2007) reported on 242 patients who underwent the Cox maze procedure (154 with the classic "cut-and-sew" [Cox maze III] procedure, 88 in whom RFA replaced the incisions of the classic procedure [Cox maze IV]) 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). Fifty-eight matched pairs were studied. At 1 year, the survival rates were 94% and 89% (p=0.19), and freedom from AF recurrence rates were 96% and 93% (p=0.52) for the Cox maze III and IV groups, respectively. The authors noted the Cox maze IV procedure was offered to higher risk patients more often than the Cox maze III procedure, which might have explained why only 58 of 88 Cox maze IV patients were matched in their analysis. The matched propensity analysis can remove measurable selection biases, but if unmeasured factors lead surgeons to choose one surgery over the other, these factors were not accounted for in the analysis.
In a second matched analysis, Stulak et al (2007) assessed 56 patients who underwent a Cox maze IV RFA procedure at a clinic who were matched (historical controls) to 56 patients who underwent the Cox maze III procedure. Matching factors were age, sex, New York Heart Association functional class, AF type, and concomitant mitral valve surgery. Here the Cox maze IV group had greater postoperative AF (43% vs 24%), more pacemaker requirements (25% vs 5%), greater use of antiarrhythmic drugs (75% vs 25%), and fewer patients were free from AF at late follow-up (mean 8.4 months; 62% vs 92%). Again, the Cox maze IV patients had greater underlying disease (more concomitant procedures were performed).

In a second article from the same clinic, Stulak et al (2014) reported on results from an unmatched retrospective comparison of Cox maze III and IV procedures among 1540 patients who underwent surgical ablation for AF at a single institution from 1993 to 2011. Energy sources used to create lesions included "cut-and-sew" in 521 (44%), cryothermy in 267 (22%), RF in 262 (22%), and a combination of these sources in 139 (12%) patients. On multivariate analysis, Cox maze III was independently associated with lower risk of recurrent AF over a follow-up of 1 to 5 years (hazard ratio, 0.4; 95% confidence interval [CI], 0.24 to 0.69; p<0.001) and more than 5 years (hazard ratio, 0.23; 95% CI, 0.12 to 0.42; p<0.001) for all patients. This study was limited by its retrospective design and lack of propensity score matching.

**Subsection Summary: Traditional Maze vs "Modified Maze" Procedures**
There have been numerous modifications to 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 high-quality and is incomplete regarding addressing all of the possible comparisons. The limited available evidence from matched case series and a small randomized controlled trial does not indicate that there are large differences in efficacy across the different approaches.

**Maze and Related Procedures as an Adjunct to Open Heart Surgery**
The evidence on the use of maze and related procedures in addition to on-bypass surgeries being done for other reasons (eg, mitral valve replacements) consists of several RCTs evaluating AF ablation when performed as an add-on for patients undergoing open heart surgery and systematic reviews of these trials.

**Review of Evidence**

**Systematic Reviews**
A Cochrane review by Huffman et al (2016) evaluated the evidence on concomitant AF surgery for patients undergoing cardiac surgery. Included were 22 trials that compared the effect of AF surgery with no AF surgery in adults undergoing cardiac surgery for another indication. Three trials used a "cut-and-sew" technique, three trials used microwave ablation, two trials used
cryoablation, and the remainder used RFA. All trials were considered at high-risk of bias. There was moderate-quality evidence that AF surgical interventions increased freedom from AF, atrial flutter, and atrial tachycardia when patients were off antiarrhythmic medications (51.0% vs 24.1%; relative risk [RR], 2.04; 95% CI, 1.63 to 2.55), but the effect on all-cause mortality was uncertain, and these procedures increased the likelihood of permanent pacemaker implantation (6% vs 4.1%; RR=1.69; 95% CI, 1.12 to 2.54).

Phan et al (2014) reported on the results of a systematic review and meta-analysis of RCTs comparing surgical ablation with no ablation among patients who had AF and were undergoing mitral valve surgery. Nine studies were selected and analyzed: five evaluated RFA, two evaluated Cox maze "cut-and-sew," one evaluated cryoablation, and one evaluated pulmonary vein isolation and Cox maze "cut-and-sew." In pooled analysis, the risk of 30-day all-cause mortality did not differ significantly between the ablation (4.4%) and nonablation (2.7%) groups (odds ratio, 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 group that received mitral valve repair plus surgical ablation (67.9%) than the group that received mitral valve repair only (17.0%; odds ratio, 13.96; 95% CI, 6.29 to 30.99; p<0.001); similarly, at 3-, 6-, 12-, and beyond 12-month follow-ups, a greater proportion of the surgical ablation group was in sinus rhythm.

In an earlier systematic review, Reston and Shuhaiber (2005) reviewed 4 RCTs and 6 comparative studies to determine whether a concurrent mitral valve surgery and maze procedure would reduce the risk of stroke or death in patients with chronic or paroxysmal AF. They found a reduction in stroke rates and a small increased risk in the need for pacemakers among patients receiving simultaneous maze procedures. Also, they noted that alternative energy sources (eg, RF) might reduce the risk of postoperative bleeding associated with classic maze incisions.

**Randomized Controlled Trials**

Some of the larger RCTs evaluating AF ablation in conjunction with open surgery and included in the 2016 Cochrane review are described below.

Gillinov et al (2015) published results of a large controlled trial that randomized 260 patients with persistent or long-standing AF who required mitral valve surgery to ablation (either pulmonary vein isolation or ablation with a maze lesion set) during surgery (n=133) or to no ablation (n=127). Compared with controls, significantly more patients in the ablation group were free from AF at both 6 and 12 months (63.2% vs 29.4%, p<0.001). The relative success ratio (ablation group vs control group) was 2.15 (95% CI, 1.54 to 3.00) on the basis of observed data. At 1 year, mortality rates did not differ significantly between the ablation group (6.8%) and the control group (8.7%; p=0.57). A composite safety endpoint did not differ significantly between groups at 30 days, nor did serious adverse event rates at 1 year.
Budera et al (2012) reported on an RCT that randomized 224 patients from 3 clinical centers to cardiac surgery plus ablation or to cardiac surgery alone. Patients were eligible for inclusion if they had at least two documented episodes of AF in the last six 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 1 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 postsurgery. 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) of patients in the surgery alone group. Adverse event rates were similar in both groups at 30 days and at 1-year follow-up. Secondary clinical outcomes, including mortality and New York Heart Association functional class, did not differ between groups at one year.

Van Breugel et al (2010) evaluated changes in quality of life in a related patient population. One hundred fifty patients with AF who were scheduled to undergo valve surgery or CABG surgery were randomized to surgery alone or surgery plus a modified maze procedure. The primary endpoint was quality of life, as measured by the 36-Item Short-Form Health Survey, the EuroQoL-5D, and the Multidimensional Fatigue Inventory. A total of 132 patients had usable survey results. Both groups improved on all quality of life measures, but in general, there were no significant differences between groups. The only exception was on the EuroQoL-5D pain/discomfort subscale, which showed a greater degree of worsening in the control group than in the maze group.

**Nonrandomized Comparative Studies**

Saint et al (2013) attempted to quantify the incremental risk conferred by adding a Cox maze IV procedure to open mitral valve 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). The operative mortality rate for the mitral valve procedure alone was predicted for each group based on the Society of Thoracic Surgeons Risk Calculator; the risk attributed to the addition of the Cox maze IV procedure was calculated by comparing the predicted mortality rate 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 regarding medical comorbidities and etiology of the mitral valve disease. The observed 30-day mortality rate 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 rate for patients who underwent a concomitant Cox maze IV procedure and mitral valve surgery was 2.9%. The Society of Thoracic Surgeons calculator predicted the 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). Interpretation of this study was limited because patients who received concomitant Cox maze IV procedures
with mitral valve surgery were from a select low-risk population; however, findings did suggest that in the appropriate patient population, the Cox maze IV procedure can be added to mitral valve 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, Kim et al (2007) reported on long-term outcomes after 127 Cox maze cut-and-sew procedures in conjunction with mitral valve replacement. Patient disposition was well-documented in the analysis. Thirty percent of patients experienced late AF recurrence at a mean of 44 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 (2013, 2014) 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.

**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 with little additional risk. Evidence from RCTs assessing open heart surgery plus surgical treatment of AF vs surgery alone has established 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 Atrial Fibrillation**

**Clinical Context and Therapy Purpose**

The purpose of maze and related procedures as a stand-alone treatment in patients who have AF is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does using maze and related procedures as a stand-alone treatment improve the net health outcome in patients who have AF?

The following PICO was used to select literature to inform this review:

**Patients**

The relevant population of interest is individuals with symptomatic drug-resistant atrial fibrillation or flutter not undergoing cardiac surgery with bypass
**Interventions**
The relevant interventions of interest are stand-alone minimally invasive, off-pump thoracoscopic maze procedures.

**Comparators**
The relevant comparators of interest are medical management or catheter ablation.

**Outcomes**
Relevant outcomes of interest are overall survival, medication use, and treatment-related morbidity. Although freedom from AF is an important outcome following AF treatment procedures, the evaluation of stand-alone maze and related procedures also requires assessment of surgery-related complications.

**Study Selection Criteria**
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Studies with duplicative or overlapping populations were excluded.

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 also requires assessment of surgery-related complications.

The evidence on the use of maze and related procedures as stand-alone 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 and endocardial procedures and are discussed separately.

**Review of Evidence**

**Systematic Reviews**
A number of systematic reviews, using different inclusion criteria, have assessed the evidence on stand-alone surgical ablation.

Van Laar et al (2017) reported on a meta-analysis of stand-alone thoracoscopic maze procedures for the treatment of AF. Reviewers included 14 studies (3
RCTs, 7 prospective cohort studies, 11 observational studies; total n=1171 patients. All studies used RFA and included bilateral pulmonary vein isolation and left atrial appendage exclusion or removal. The pooled drug-free success rate at 1 year was 77% (95% CI, 72% to 83%), with a similar success rate at 2 years. Subgroup analysis of the type of AF showed the highest success rate for paroxysmal AF at 81% (95% CI, 73% to 86%). The in-hospital complication rate was 2.9% and included conversion to sternotomy, rethoracotomy due to excess bleeding, pulmonary problems, stroke, and pacemaker implantation, pneumonia, and reintubation for hypoxia.

Phan et al (2016) conducted a systematic review of studies comparing thoracoscopic surgical ablation with catheter ablation, including the Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment (FAST) trial. Eight comparative studies, with a total of 321 video-assisted thoracoscopic surgical ablation patients and 378 catheter ablation patients, met inclusion criteria. For the review's primary efficacy endpoint of freedom from AF without the use of antiarrhythmic drugs, the treatment success was significantly higher in the surgical ablation group (81%) than in the catheter ablation group (64.3%) at 6 months postprocedure (RR=1.23; 95% CI, 1.02 to 1.49; p=0.03). This difference was maintained at 12 months postprocedure. Patients treated with surgical ablation had significantly higher rates of major complications (including death, stroke, transient ischemic attack, major bleeding, 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 by La Meir et al (2013). Reviewers noted substantial differences in patient populations, surgical techniques, and outcome definitions across studies. At 1 year, the range of success, as defined by freedom from AF while off all medications, was 51% to 86%. Outcomes for RFA appeared superior to those using ultrasound or microwave energy sources. Reviewers also noted that success was higher for the population of patients who had paroxysmal AF compared with those who had persistent and permanent AF. Early complication rates 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.

**Randomized Controlled Trials**

The FAST RCT, reported by Boersma et al (2012) provides most of the direct evidence comparing surgical AF ablation to catheter ablation (Table 3). FAST compared stand-alone surgical ablation with percutaneous ablation. This 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 thoracoscopy under general anesthesia or to percutaneous catheter ablation. Both techniques used RF
energy. All patients in the surgical ablation group also had their left atrial appendage removed. The primary outcome was freedom from AF while off all antiarrhythmic medications during 12 months of follow-up. Secondary outcomes were freedom from AF, including patients still on medications and adverse events. Prior unsuccessful catheter ablation had been performed in 67% of patients.

At 1 year, (Table 4) freedom from AF while off all antiarrhythmic drugs was achieved by 65.6% (40/61) of the surgical ablation group compared with 36.5% (23/63) of the catheter ablation group (p=0.002). Freedom from AF, on or off medications, was achieved by 78.7% (48/61) of the surgical ablation group compared with 42.9% (27/63) of the catheter ablation group (p<0.001). Serious adverse events were more common in the surgical group (23.0% [14/61]) than in the catheter ablation group (3.2% [2/63]; p=0.001). In each group, there was one episode of tamponade and stroke. Additional complications in the surgical group included six patients with pneumothorax, two who required pacemaker insertion, and one patient each who had hemothorax, rib fracture, pneumonia, or required sternotomy for bleeding. In 2019, Castella et al (2019) reported extended follow-up of patients randomized in the FAST trial.\textsuperscript{22} After a mean follow-up of 7.0 years from randomization, recurrence of atrial arrhythmias was significantly lower in the thoracoscopic ablation group compared to the catheter ablation group (56% [34/61] versus 87% [55/63]; adjusted HR 0.40, 95% CI 0.25-0.64; P<0.001). Additional ablation procedures were more common in the catheter ablation group (49% versus 13%; P<0.001). Rates of the composite outcome of death, MI, or cerebrovascular event (transient ischaemic attack, ischaemic or haemorrhagic stroke) were similar between groups (15% following thorascoscopy [9/61] and 16% following catheter ablation [10/63]; adjusted HR for time to first event 1.11; 95% CI 0.40-3.10). Although encouraging, due to important study conduct limitations including inadequate control for selection bias (i.e., fewer patients with persistent AF patients in the thoracoscopic ablation group), insufficient power to detect a difference in clinical outcomes, and lack of data on type of arrhythmia recurrence, further RCT data are required to verify these findings.

In a subsequent smaller RCT, Pokushalov et al (2013) randomized patients with a prior failed first catheter ablation procedure for AF to repeat catheter ablation (n=32) or to surgical ablation with video-assisted thoracoscopy (n=32).\textsuperscript{23} After 12 months, a higher proportion of patients who underwent surgical ablation were free of AF and 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).

Additionally, Adiyaman et al (2018) published results of a small, single-center randomized controlled trial that compared minimally invasive thoracoscopic pulmonary vein isolation with left atrial appendage ligation (surgical MIPI) to percutaneous CA in 52 patients with symptomatic paroxysmal or early persistent AF (continuous AF duration, <3 months) with failure of at least 1 class 1 or 3 antiarrhythmic drugs, but no previous CA.\textsuperscript{24} An implantable loop recorder was
used for follow-up continuous rhythm monitoring for 2 years. In contrast to the previously discussed RCTs such as FAST that found better efficacy with surgical ablation, this RCT found no difference in arrhythmia-free survival between the CA and MIPI groups (56% versus 29.2%; HR 0.56, 95% CI, 0.26-1.20) and major complications were greater in the MIPI group (20.8% in MIPI versus 0% in CA; difference, 20.8%; 95% CI, 4.8%–36.9%; P=0.029).

Table 3. Summary of Key RCT Characteristics

<table>
<thead>
<tr>
<th>Study; Trial</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boersma (2012); FAST</td>
<td>EU</td>
<td>2</td>
<td>2007-2010</td>
<td>Individuals with symptomatic AF for at least 1 year and had failed at least 1 antiarrhythmic medication; 67% prior failed catheter ablation</td>
<td>Stand-alone surgical ablation, N=63</td>
</tr>
<tr>
<td>Pokushalov (2013)</td>
<td>Russia</td>
<td>1</td>
<td>2011-2013</td>
<td>Individuals with history of symptomatic PAF/PersAF after a previous failed first RF ablation procedure</td>
<td>Stand-alone surgical ablation, N=32</td>
</tr>
<tr>
<td>Adiyaman (2018)</td>
<td>The Netherlands</td>
<td>1</td>
<td>Not reported</td>
<td>Individuals with symptomatic PAF or early PersAF (continuous AF duration, &lt;3 months) with failure of at least 1 class 1 or 3 antiarrhythmic drugs, but no previous CA</td>
<td>Stand-alone surgical ablation, N=26</td>
</tr>
</tbody>
</table>

RCT: randomized controlled trial; FAST: Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment; EU: Europe; PAF: paroxysmal atrial fibrillation; PersAF: persistent atrial fibrillation; CA: catheter ablation

Table 4. Summary of Key RCT Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Freedom from AF while off all</th>
<th>Mortality</th>
<th>Serious Adverse</th>
<th>Recurrence of atrial arrhythmias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Populationa</td>
<td>Interventionb</td>
<td>Comparatorc</td>
<td>Outcomesd</td>
</tr>
<tr>
<td>---------------------</td>
<td>----------------</td>
<td>---------------</td>
<td>-------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Boersma (2012); FAST²¹</td>
<td>4. Most patients had undergone a prior unsuccessful catheter ablation and had paroxysmal atrial fibrillation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical ablation</td>
<td>1-year</td>
<td>1-year</td>
<td>1-year</td>
<td>7-years</td>
</tr>
<tr>
<td>Catheter ablation</td>
<td>36.5% (23/63)</td>
<td>1.6% (1/63)</td>
<td>3.2% (2/63)</td>
<td></td>
</tr>
<tr>
<td>Relative measure</td>
<td>P=0.002</td>
<td>Not reported</td>
<td>P=0.001</td>
<td>HR 0.40, 95% CI 0.25–0.64; P&lt;0.001</td>
</tr>
<tr>
<td>Surgical ablation</td>
<td>81% (26/32)</td>
<td>0</td>
<td>7¹</td>
<td>3% (1/32)</td>
</tr>
<tr>
<td>Catheter ablation</td>
<td>47% (15/32)</td>
<td>0</td>
<td>9% (3/32)</td>
<td></td>
</tr>
<tr>
<td>Surgical ablation</td>
<td>29.2%</td>
<td>0</td>
<td>NR</td>
<td>20.8%</td>
</tr>
<tr>
<td>Catheter ablation</td>
<td>56%</td>
<td>0</td>
<td>NR</td>
<td>0%</td>
</tr>
<tr>
<td>Relative measure</td>
<td>HR 0.56; 95% CI, 0.26–1.20</td>
<td>N/A</td>
<td>NR</td>
<td>Difference, 20.8%; 95% CI, 4.8%–36.9%</td>
</tr>
</tbody>
</table>

¹Number of events
CI: confidence interval; HR: hazard ratio; RCT: randomized controlled trial; N/A: Not Applicable; NR: Not Reported

Table 5. Study Relevance Limitations of Key RCTs
ECG: Electrocardiography; HRS: Heart Rhythm Society; RCT: randomized controlled trial.
The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

a Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

 Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

### Table 6. Study Design and Conduct Limitations of Key RCTs

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation(^a)</th>
<th>Blinding(^b)</th>
<th>Selective Reporting(^c)</th>
<th>Data Completeness(^d)</th>
<th>Power(^e)</th>
<th>Statistical(^f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boersma (2012); FAST(^24)</td>
<td>4. Surgical patients had more paroxysmal AF (74% vs 59%), both as the initial diagnosis and in the preprocedural Holter recording, with a lower CHADS2 score and more prior failed ablation (74% vs 63%) and had fewer males (74% vs 87%)</td>
<td>1. Not blinded to treatment assignment; 2. Not blinded outcome assessment</td>
<td>1. Not blinded to treatment assignment; 2. Not blinded outcome assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Nonrandomized Comparative Studies

Several small, single-center observational studies have compared maze and related minimally invasive surgical ablation procedures as a stand-alone treatment for AF to matched comparison groups of patients who received catheter ablation (Tables 7 and 8). These case series with matched control groups offer stronger evidence for comparative efficacy than do single-arm case series. Studies varied in the prognostic variables used to match the patient groups, the type of surgical ablation used, the proportion of patients with prior failed catheter ablation (0% to 100%), and follow-up duration. All studies consistently found higher success rates with surgical ablation. Although findings from these small pilot studies are promising, their interpretation is restricted by important
methodological limitations. For example, they did not calculate the comparative treatment risk of serious adverse events. Additionally, as these studies involved small series of patients treated over a decade ago in single centers, the relevance to modern-day CA techniques across a broader range of settings is unclear.

Table 7. Summary of Characteristics of Comparative Observational Studies with Matched Comparison Groups

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Type</th>
<th>Country</th>
<th>Dates</th>
<th>Participants</th>
<th>Surgical Ablation Type</th>
<th>Catheter Ablation</th>
<th>Follow-Up</th>
<th>Matching variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mahapatra (2011)(^25)</td>
<td>Case series with matched control groups</td>
<td>US</td>
<td>2007-2009</td>
<td>Persistent or LSP AF who have failed ≥ 1 prior CA</td>
<td>Combined epicardial-surgical and endocardial-catheter, N=15</td>
<td>CA, N=30</td>
<td>20.7 m</td>
<td>LA size by echo, AF duration, AF type, use of post-ablation AAD, lack of prior cardiac surgery, and left ventricular ejection fraction</td>
</tr>
<tr>
<td>Stulak (2011)(^26)</td>
<td>Case series with matched control groups</td>
<td>US</td>
<td>1993-2007</td>
<td>Lone AF, 10% with prior CA</td>
<td>Isolated biatrial cut-and sew Cox-Maze III procedure, N=97</td>
<td>CA, N=194</td>
<td>5.6 y for SA; 3.1 y for CA</td>
<td>Median age, age range, male, intermittent AF</td>
</tr>
<tr>
<td>Wang (2011)(^27)</td>
<td>Case series with matched control groups</td>
<td>China</td>
<td>2006-2009</td>
<td>Long-standing persistent AF (i.e., continuous AF for ≥ 1 year), resistant to either electrical or pharmacological cardioversion; no previous CA</td>
<td>Video-assisted minimally invasive ablation, N=83</td>
<td>CA, N=83</td>
<td>2.2 y</td>
<td>AF duration, left atrial dimension and sex</td>
</tr>
</tbody>
</table>

LSP: long-standing persistent; CA: catheter ablation; AF: atrial fibrillation; LA: left atrial; AAD: anti-arrhythmic drug; M: month; Y: year; US: United States

Table 8. Summary of Results of Comparative Observational Studies with Matched Comparison Groups

<table>
<thead>
<tr>
<th>Study</th>
<th>Free of atrial freedom</th>
<th>Need for death</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Other observational studies have reported outcomes for stand-alone AF treatment. Representative studies are described next. In a retrospective cohort study, Lawrance et al (2014) compared patients who underwent a Cox maze IV procedure either by right mini-thoracotomy (n=104) or sternotomy (n=252) at a single-center from 2002 to 2014. Freedom from atrial tachyarrhythmias off antiarrhythmic drugs did not differ significantly between groups. The overall complication rate was lower in the mini-thoracotomy group (6%) than in the sternotomy group (13%; p=0.044).

De Maat et al (2013) 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. Patients were treated 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 (17%) patients had had transcatheter ablation performed. The percentages of patients free from atrial arrhythmias without the use of antiarrhythmic drugs were 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 three sternotomy or mini-thoracotomy procedures due to complications, two cases of late pericardial tamponade, one case of pericardial effusion requiring video-assisted thoracoscopic surgery, and one stroke.

Massimiano et al (2013) reported on 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). Among the 115 patients who underwent AF ablation, the percentages of patients in sinus rhythm at 6, 12, and 24 months were 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 were 85%, 85%, and 77%, respectively.

**Single-Arm Studies**
Numerous single-arm case series have reported high success rates following a minimally invasive surgical procedure; however, these case series offer limited evidence of the efficacy of the procedure itself. Most series lacked a control group, generally only reported short-term outcomes, and did not consistently report adverse events. For example, Vos et al (2020) reported on outcomes for 82 consecutive patients that underwent totally thoracoscopic ablation including left appendage closure. While it is encouraging that after a mean follow-up of 4.0 years, 60% of patients were free from atrial arrhythmia, long-term complications were not studied.

Several single-arm case series of minimally invasive epicardial ablation have reported on 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 fewer treatment options and is more likely to benefit from surgical procedures. However, these studies only offer very limited evidence of the comparative efficacy of alternatives such as catheter ablation. For example, Ad et al (2011) reported on 40 patients who had failed catheter ablation, with a mean of 2.3 prior ablations per patient. The percentages of patients maintaining sinus rhythm at 6, 12, and 24 months were 76% (29/38), 89% (23/26), and 93% (13/14), respectively. Castella et al (2010) enrolled 34 patients who had failed a mean of 2 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.

**Section Summary: Maze and Related Procedures as a Stand-Alone Treatment for Atrial Fibrillation**
The evidence on the role of maze and related procedures as stand-alone options consists of three RCTs (including the FAST study) and many case series, some with matched control groups. The RCTs have had mixed results. RCTs (including the FAST study) with a large proportion of patients with unsuccessful previous CA reported higher success rates in maintaining sinus rhythm at one-year follow-up
with thoracoscopic ablation and lower 7-year recurrence of atrial arrhythmias, but have also reported higher adverse event rates than catheter ablation. In contrast, a small single-center RCT of patients with no previous CA found no significant benefit from a stand-alone minimally invasive thoracoscopic procedure. This evidence does not support the superiority of one technique over the other but suggests that other factors (eg, type of AF, prior treatments, inability to take anticoagulation, patient preference) may influence the decision for the type of procedure. Case series with matched control groups have also reported higher success rates in maintaining sinus rhythm compared with catheter ablation. The single-arm case series have corroborated the high success rates following surgical treatment but do not provide sufficient evidence to form conclusions on the comparative efficacy of surgical treatment vs other treatments.

Some case series and an RCT have included only patients who have failed previous catheter ablation. These studies have also reported high success rates following thoracoscopic ablation, suggesting that patients who fail catheter ablation may still benefit from thoracoscopic ablation. However, the RCT reported higher adverse event rates than catheter ablation, and the risk-benefit ratio is not well-defined.

**Hybrid Thoracoscopic and Endocardial Ablation Procedures**

**Clinical Context and Therapy Purpose**
The purpose of hybrid thoracoscopic and endocardial ablation procedures in patients who have AF is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does using hybrid thoracoscopic and endocardial ablation procedures improve the net health outcome in patients who have AF?

The following PICO was used to select literature to inform this review:

**Patients**
The relevant population of interest is individuals with symptomatic drug-resistant atrial fibrillation or flutter not undergoing cardiac surgery with bypass

**Interventions**
The relevant interventions of interest are hybrid thoracoscopic and endocardial ablation procedures

**Comparators**
The relevant comparators of interest are medical management or catheter ablation

**Outcomes**
Relevant outcomes of interest are overall survival, medication use, and treatment-related morbidity.
Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews
Je et al (2015) reported on 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. Selected were 2 studies on minimally invasive endocardial Cox maze procedure (n=145 patients), 26 on epicardial surgical ablation (n=1382 patients), and 9 on hybrid surgical ablation (n=350 patients). No statistical analyses or meta-analyses were possible due to the heterogeneity in methodologies and data reporting. However, reviewers did 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.

Nonrandomized Studies
La Meir et al (2012) reported on a comparative study that enrolled 35 patients who underwent a hybrid procedure and 28 patients who underwent a standard percutaneous procedure. Approximately two-thirds (42/63) of the patients had a previous percutaneous ablation procedure. At 1 year, there were more patients in the hybrid group who were free of AF, but this difference was not statistically significant (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). Significantly more patients in the hybrid group were on warfarin at 1 year (29% vs 13.4%, p<0.001). There was no difference between groups on the frequency of adverse events.

Observational Studies
Other relevant single-arm case series have included populations ranging from 19 to 104 patients. These series have consistently reported high success rates in maintaining sinus rhythm at 1-year follow-up, ranging from 71% to 91%. Some series have reported individual adverse events, but did so variably not systematically, resulting in an inability to accurately estimate adverse event rates.
Section Summary: Hybrid Thoracoscopic and Endocardial Ablation Procedures

The evidence on hybrid ablation consists of a nonrandomized comparative study that compared a hybrid procedure to a standard percutaneous procedure and a number of single-arm case series and a systematic review of these studies. The studies have suggested 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 to permit assessment of the benefits and harms of hybrid ablation procedures compared with alternatives.

Summary of Evidence

For individuals who have symptomatic AF or flutter who are undergoing cardiac surgery with bypass who received a Cox maze or a 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. Several small RCTs have provided most of the direct evidence confirming the benefit of a modified maze procedure for patients with AF who are undergoing mitral valve surgery. These trials have established that the addition of a modified maze procedure results in a lower incidence of atrial arrhythmias following surgery, with minimal additional risks. Observational studies have supported these RCT findings. The evidence is sufficient to determine 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. Most of the direct evidence comparing surgical AF ablation with percutaneous catheter ablation comes from one RCT (FAST) that used video-assisted thoracoscopy in patients with antiarrhythmic drug-refractory atrial fibrillation with left atrial dilatation and hypertension, 67% of which had previously failed CA. In FAST, at one year, thoracoscopic ablation had higher success at maintaining sinus rhythm (36.5% for CA and 65.6% for surgical ablation), but also reported higher adverse event rates compared with CA. At 7 years, outcomes were consistently improved with thoracoscopic ablation, but interpretation of those findings is limited by important flaws in study conduct. In contrast, findings from a small single-center RCT in patients with no previous CA suggested no significant benefit with minimally invasive thoracoscopic ablation and more major complications. The case series have generally reported high success rates, and a few with matched comparison groups have reported higher success rates with surgical treatment than with catheter ablation. However, most series lacked a control group, generally only reported short-term outcomes, and did not consistently report adverse events. Therefore, this evidence does not permit definitive conclusions whether a specific 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. 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 and endocardial ablation procedures, the evidence includes a nonrandomized comparative study and single-arm case series. Relevant outcomes are overall survival, medication use, and treatment-related morbidity. The studies have suggested 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 to permit direct comparisons of the benefits and harms of hybrid ablation procedures with alternatives. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

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

2013 Input
In response to requests, input was received from 2 physician specialty societies and 6 academic medical centers (4 reviewers) while this policy was under review in 2013. There was consensus on the medically necessary statements. For subgroups of populations (eg, those who have failed percutaneous catheter ablation), there was mixed support without consensus. There was also mixed support for the use of hybrid ablation.

2010 Input
In response to requests, input was received from 1 physician specialty society and 3 academic medical centers (4 reviewers) while this policy was under review in 2010. There was unanimous support for the policy statement regarding with cardiopulmonary bypass maze procedure. There was mixed support for the policy statement on off-bypass (off-pump) maze procedure; some providing input indicated off-pump procedures might be useful in select patients (eg, those who cannot tolerate anticoagulation). Several providing input also commented on the limited long-term data for off-pump procedures.

Practice Guidelines and Position Statements
Society of Thoracic Surgeons
In 2017, the Society of Thoracic Surgeons published guidelines on the surgical treatment of atrial fibrillation (AF). Recommendations are provided in see Table 9.

Table 9. Guidelines on Surgical Treatment of Atrial Fibrillation

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical ablation for AF is recommended at the time of concomitant mitral operations to restore sinus rhythm.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Surgical ablation for AF is recommended at the time of concomitant isolated aortic valve replacement, isolated CABG surgery, and aortic valve replacement plus CABG operations to restore sinus rhythm.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Surgical ablation for symptomatic AF in the absence of structural heart disease that is refractory to class I/III antiarrhythmic drugs or catheter-based therapy of both is reasonable as a primary stand-alone procedure to restore sinus rhythm.</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

AF: atrial fibrillation; CABG: coronary artery bypass graft; COR: class of recommendation; LOE: level of recommendation.

American Heart Association et al
In 2019, the American Heart Association, American College of Cardiologists, and Heart Rhythm Society issued joint guidelines in collaboration with the Society of Thoracic Surgeons on the management of patients with AF. Recommendations on the use of surgical ablation to maintain sinus rhythm are provided in Table 10.

Table 10. Guidelines on the Management of Atrial Fibrillation

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot; AF catheter ablation may be reasonable in selected patients with symptomatic AF and HF with reduced left ventricular (LV) ejection fraction (HFrEF) to potentially lower mortality rate and reduce hospitalization for HF (S6.3.4-1, S6.3.4-2).&quot;</td>
<td>IIb</td>
<td>B-R</td>
</tr>
</tbody>
</table>

AF: atrial fibrillation; COR: class of recommendation; LOE: level of recommendation.

Heart Rhythm Society et al
A 2017 expert consensus statement was developed by the Heart Rhythm Society, European Heart Rhythm Association, and European Cardiac Arrhythmia Society. The statement was endorsed by four other cardiology associations. Recommendations on concomitant surgical ablation in patients undergoing cardiac surgery for other purposes and who have symptomatic AF are provided in Table 11.

Table 11. Guidelines on Concomitant Surgical Ablation in Patients Undergoing Cardiac Surgery

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal: Surgical ablation is recommended for patients undergoing surgery for other indications</td>
<td>II</td>
<td>B-NR</td>
</tr>
<tr>
<td>Persistent: Surgical ablation is recommended for patients undergoing surgery for other indications</td>
<td>II</td>
<td>B-NR</td>
</tr>
<tr>
<td>Longstanding Persistent: Surgical ablation is recommended for patients undergoing</td>
<td>II</td>
<td>NR</td>
</tr>
</tbody>
</table>
surgery for other indications

COR: class of recommendation; LOE: level of recommendation; NR: nonrandomized.

a: For patients with symptomatic AF prior to initiation of antiarrhythmic therapy with Class I or III antiarrhythmic medication and indication for concomitant closed surgical ablation for AF, paroxysmal, persistent, and long-standing persistent is reasonable (Class: IIa; LOE: B-NR).

The following recommendations were made on stand-alone surgical ablation in patients with symptomatic AF refractory or intolerant to at least one class 1 or 3 antiarrhythmic medication (see Table 12).

Table 12. Guidelines on Stand-Alone Surgical Ablation for Symptomatic AF trial Fibrillation Refractory to Antiarrhythmics

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach</td>
<td>IIb</td>
<td>B-NR</td>
</tr>
<tr>
<td>Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation</td>
<td>IIb</td>
<td>B-NR</td>
</tr>
<tr>
<td>Persistent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach</td>
<td>IIa</td>
<td>B-NR</td>
</tr>
<tr>
<td>Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation</td>
<td>IIa</td>
<td>B-NR</td>
</tr>
<tr>
<td>Longstanding persistent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach</td>
<td>IIb</td>
<td>B-NR</td>
</tr>
<tr>
<td>Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation</td>
<td>IIb</td>
<td>B-NR</td>
</tr>
</tbody>
</table>

COR: class of recommendation; LOE: level of recommendation; NR: nonrandomized.
a: The recommendations noted that "it might be reasonable to apply the indication for stand-alone surgical ablation described above to patients being considered for hybrid surgical AF ablation.

American Association for Thoracic Surgery

In 2017, the American Association for Thoracic Surgery published guidelines on surgical ablation for AF. Recommendations on concomitant surgical ablation in patients with AF are provided in Table 13.

Table 13. Guidelines on Concomitant Surgical Ablation in Patients with Atrial Fibrillation

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Addition of a concomitant surgical ablation procedure for AF does not increase the incidence of perioperative morbidity.&quot;</td>
<td>IIa</td>
<td>A, B-R, B-NR</td>
</tr>
<tr>
<td>&quot;Addition of a concomitant surgical ablation procedure for AF does not change the incidence of perioperative stroke/TIA.&quot;</td>
<td>IIa</td>
<td>A</td>
</tr>
</tbody>
</table>
"Addition of a concomitant surgical ablation procedure for AF does not change the incidence of late stroke/TIA, but subgroup analysis of nonrandomized controlled trials found a significant reduction in late stroke/TIA incidence." IIa A, B-NRb

"A surgical procedure that includes concomitant surgical ablation for AF does improve HRQL." IIa B-R

"Addition of concomitant surgical ablation for AF does improve AF-related symptoms, and this improvement is greater than in patients without surgical ablation for AF." IIa C-LD

"Addition of concomitant surgical ablation for AF does improve 30-day operative mortality." I A

"Addition of a concomitant surgical ablation procedure for AF improves long term survival." IIa A, B-NRc

AF: atrial fibrillation; COR: class of recommendation; HRQL: health-related quality of life; LOE: level of recommendation; NR: nonrandomized; R: randomized; TIA: transient ischemic attack
a: "LOE A for deep sternal wound infection, pneumonia, reoperation for bleeding, and renal failure requiring dialysis; LOE B-R for intensive care unit length of stay and total hospital length of stay; and LOE B-NR for readmission less than 30 days and renal failure."
b: "LOE A for no change in incidence of late stroke/TIA (up to 1 year of follow-up after surgery) and LOE B-NR for reduction in incidence of late stroke/TIA (>1 year of follow-up after surgery)."
c: "LOE A for no change in long-term survival (up to 1 year after surgery) and LOE B-NR for improvement in long-term survival (>1 year after surgery)."

Canadian Cardiovascular Society
In 2011, the Canadian Cardiovascular Society published guidelines on surgical therapy for AF.59 These guidelines stated there is a high rate of freedom from AF following surgical treatment (70%-85% at 1 year), but that surgical ablation of AF has not been shown to alter mortality rates (see Table 14).

Table 14. Guidelines on Surgical Therapy for Atrial Fibrillation

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>SOR</th>
<th>QOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>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.</td>
<td>Strong</td>
<td>Low</td>
</tr>
<tr>
<td>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.... This recommendation recognizes that left atrial endocardial access is not routinely required for aortic or coronary surgery.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
<tr>
<td>We recommend that oral anticoagulant therapy be continued following surgical AF ablation in patients with a CHADS2 score ≥2.</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

AF: atrial fibrillation; QOE: quality of evidence; SOR: strength of recommendation.
Although not a formal recommendation, these guidelines indicated that stand-alone surgical ablation should be considered after failure of prior attempts at catheter ablation and antiarrhythmic drugs.

The Society (2012) published a focused update to its comprehensive 2010 guidelines on AF. The guidelines discussed the use of anticoagulants in the treatment of AF.

**U.S. Preventive Services Task Force Recommendations**
Not applicable.

**Medicare National Coverage**
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

**Ongoing and Unpublished Clinical Trials**
Some currently unpublished trials that might influence this review are listed in Table 15.

**Table 15. Summary of Key Trials**

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02755688</td>
<td>Catheter Ablation Versus Thoracoscopic Surgical Ablation in Long Standing Persistent Atrial Fibrillation (CASA-AF)</td>
<td>120</td>
<td>Mar 2020</td>
</tr>
<tr>
<td>NCT04237389</td>
<td>Comparative Assessment of Catheter and Thoracoscopic Approaches in Patients With Persistent and Long-standing Persistent Atrial Fibrillation</td>
<td>60</td>
<td>Aug 2022</td>
</tr>
<tr>
<td><strong>Unpublished</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01319747a</td>
<td>Video-Assisted Thoracoscopic Pulmonary Vein Isolation Versus Percutaneous Catheter Ablation in Atrial Fibrillation Trial</td>
<td>77</td>
<td>Nov 2014 (terminated)</td>
</tr>
<tr>
<td></td>
<td>Success Trial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02047279</td>
<td>Left Atrium Reduction Versus no Left Atrium Reduction for Patients With Enlarged Left Atria and Persistent or Long Standing Persistent Atrial Fibrillation Undergoing Mitral Valve Surgery</td>
<td>120</td>
<td>Sep 2017 (completed)</td>
</tr>
</tbody>
</table>

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

**REFERENCES**


6. Stulak JM, Suri RM, Burkhart HM, et al. Surgical ablation for atrial fibrillation for two decades: are the results of new techniques equivalent to the Cox maze III procedure?. J Thorac Cardiovasc Surg. May 2014; 147(5): 1478-86. PMID 24560517


**Billing Coding/Physician Documentation Information**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>33254</td>
<td>Operative tissue ablation and reconstruction of atria, limited (eg, modified maze procedure)</td>
</tr>
<tr>
<td>33255</td>
<td>Operative tissue ablation and reconstruction of atria, extensive (eg, maze procedure); without cardiopulmonary bypass</td>
</tr>
<tr>
<td>33256</td>
<td>Operative tissue ablation and reconstruction of atria, extensive (eg, maze procedure); with cardiopulmonary bypass</td>
</tr>
<tr>
<td>33257</td>
<td>Operative Tissue Ablation and Reconstruction of Atria at the Time of Other Cardiac Procedure(s), Limited (List Sep)</td>
</tr>
<tr>
<td>33258</td>
<td>Operative Tissue Ablation and Reconstruction of Atria at Time of Other Procedure, Extensive, wo Bypass (List Sep)</td>
</tr>
<tr>
<td>33259</td>
<td>Operative Tissue Ablation and Reconstruction of Atria at Time of Other Procedure, Extensive, w Bypass (List Sep)</td>
</tr>
<tr>
<td>33265</td>
<td>Endoscopy, surgical; operative tissue ablation and reconstruction of atria, limited (eg, modified maze procedure), without cardiopulmonary bypass</td>
</tr>
<tr>
<td>33266</td>
<td>Endoscopy, surgical; operative tissue ablation and reconstruction of atria, extensive (eg, maze procedure), without cardiopulmonary bypass</td>
</tr>
<tr>
<td>33999</td>
<td>Unlisted procedure, cardiac surgery</td>
</tr>
</tbody>
</table>

**ICD-10 Codes**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I48.0-I48.1</td>
<td>Atrial fibrillation and flutter code range</td>
</tr>
</tbody>
</table>

The Hybrid ablation technique would be billed using the unlisted code for cardiac surgery (33999).

**Additional Policy Key Words**

- Maze procedure
- Modified maze procedure

**Policy Implementation/Update Information**

- 1/1/08 New policy.
- 1/1/09 No policy statement changes.
- 1/1/10 No policy statement changes.
- 1/1/11 No change in policy statements. Title revised, previously titled Maze Procedures.
- 1/1/12 No policy statement changes.
- 6/1/12 No policy statement changes.
- 6/1/13 No policy statement changes.
6/1/14  Investigational statement added for hybrid ablation. Updated Description to include different techniques.

6/1/15  No policy statement changes.

8/1/15  The phrase “without concomitant cardiac surgery” was removed from the medical necessary policy statement for maze or modified maze during cardiopulmonary bypass, with addition of “not medically necessary” statement for Maze done without concurrent cardiac surgery.

8/1/16  No policy statement changes.

8/1/17  “Drug resistant” removed from medically necessary statement. “Symptomatic, drug-resistant “removed from not medically necessary statement.

8/1/18  No policy statement changes.

8/1/19  No policy statement changes.

8/1/20  No policy statement changes.

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