Medical Policy

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

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Populations	Interventions	Comparators	Outcomes
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 who are 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 who are 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

DESCRIPTION

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.

OBJECTIVE

The objective of this evidence review is to determine whether maze or modified maze procedures improve the net health outcome when performed in patients with atrial fibrillation in combination with cardiac procedures or as a stand-alone treatment.

BACKGROUND

Atrial Fibrillation

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 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 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

Device	Manufacturer	510(k)/Premarket Approval Date	510(k)/Premarket Approval Number
EPi-Sense Guided Coagulation System	Atricure	April 2021	P200002
Medtronic DiamondTemp™ System	Medtronic	Jan 2021	P200028
Cobra Fusion Ablation System	AtriCure	Feb 2019	K190151
Medtronic Cardioblate® System	Medtronic	Jan 2002	K013392
Cardima Ablation System	Cardima	Jan 2003	K022008
Epicor™ Medical Ablation System	Epicor Medical	Feb 2004	K022894
Isolator™ Transpolar™ Pen	AtriCure	Jun 2005	K050459
Estech COBRA® Cardiac Electrosurgical Unit	Endoscopic Technologies	Jan 2006	K053326
Coolrail™ Linear Pen	AtriCure	Mar 2008	K073605
Numeris® Guided Coagulation System with VisiTrax®	nContact Surgical	Feb 2009	K090202
EPi-Sense® Guided Coagulation System with VisiTrax®	nContact Surgical	Nov 2012	K120857

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

Device	Manufacturer	510(k)/Premarket Approval Date
Cryocare® Cardiac Surgery System	Endocare	Mar 2002
SeedNet™ System	Galil Medical	May 2005
SurgiFrost® XL Surgical CryoAblation System	CryoCath Technologies; now Medtronic	Jul 2006
Isis™ cryosurgical unit	Galil Medical	Mar 2007
Artic Front Advance™ and Arctic Front Advance Pro™ and the Freezer Max™ Cardiac Cryoablation Catheters	Medtronic	Jun 2020

POLICY

A. 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.

B. Minimally invasive, off-pump maze procedures (i.e., modified maze procedures), including those done via mini-thoracotomy, are considered **experimental / investigational** for treatment of atrial fibrillation or flutter.

C. Hybrid ablation (defined as a combined percutaneous and thoracoscopic approach) is considered **experimental / investigational** for the treatment of atrial fibrillation or flutter.

D. 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.

Policy Guidelines

1. Given the availability of less-invasive alternative approaches to treat atrial fibrillation, performing the maze procedure without concomitant cardiac surgery should rarely be needed.
2. Published studies on the maze procedure have described patients with drug-resistant AF and atrial flutter as having experienced their arrhythmias for an average of 7 or more years and having had unsuccessful results with an average of 5 or more antiarrhythmic medications.

RATIONALE

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through April 7, 2021.

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, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 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. Randomized controlled trials 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 atrial fibrillation (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:

Populations

The relevant population of interest is individuals with symptomatic AF or flutter who are undergoing cardiac surgery with bypass.

Interventions

The therapies being considered are Cox maze or modified maze procedures added to on-bypass surgeries.

Comparators

The following practice is currently being used to treat individuals with symptomatic AF or flutter who are undergoing cardiac surgery with bypass: medical management or catheter ablation (CA).

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

TRADITIONAL MAZE VERSUS "MODIFIED MAZE" PROCEDURES

Systematic Reviews

Khargi et al (2005) analyzed 48 studies comprising 3832 patients who received surgical treatment for AF using the classic "cut-and-sew" Cox maze III technique or an alternative source of energy.[1,] 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.[2,]

Randomized Controlled Trials

Subsequent to the systematic review described above, Zhang et al (2020) published results of a RCT that randomized 120 patients who underwent valve surgery and bipolar radio frequency ablation (RFA) 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).[3,] 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% vs 60.0%; hazard ratio [HR], 0.71, 95% confidence interval [CI], 0.39 to 1.32), late mortality (3.3% vs 6.0%; HR 0.5, 95% CI, 0.09 to 2.71), or cumulative major adverse events (16.7% vs 23.3%; HR 0.68, 95% CI, 0.30 to 1.52). However, a larger, multicenter RCT is still needed to confirm these findings.

Han et al (2020) completed a randomized, single-center, noninferiority trial that evaluated the efficacy and safety of the classic "cut-and-sew" Maze technique (n=100) as compared to the Maze performed by cryoablation (CryoMaze; n=100) technique in patients undergoing mitral valve surgeries.[4,] All enrolled patients had persistent or long-standing persistent AF. The primary endpoint was freedom from AF off antiarrhythmic drugs at 12 months. Secondary endpoints included freedom at 3 and 6 months and a composite of serious adverse events. Results revealed that freedom from AF at 12 months was achieved in 85% (95% CI, 0.76 to 0.91) of patients in the CryoMaze group as compared to 88% (95% CI, 0.80 to 0.94) of patients in the "cut-and-sew" Maze group. Cryomaze met the criteria for noninferiority for this endpoint (p value for noninferiority =.0065). Similar outcomes were observed for freedom from AF at 3 months (80% CryoMaze vs. 79% "cut-and-sew"; p value for noninferiority =.0025) and 6 months (84% CryoMaze vs. 88% "cut-and-sew"; p value for noninferiority =.0124). No significant difference in serious adverse effects was noted between groups (12 CryoMaze vs. 17 "cut-and-sew"; p=.315); however, perioperative bleeding, length of surgery, intensive care unit stay, postoperative hospital stay, and the need for temporary pacing were all significantly reduced in the CryoMaze group.

Observational Studies

Several observational studies have compared the Cox maze III procedure with other procedures (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).[5,] Fifty-eight matched pairs were studied. At 1 year, the survival rates were 94% and 89% (p=.19), and freedom from AF recurrence rates were 96% and 93% (p=.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 1 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.[5,] 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 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.[6,]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 a lower risk of recurrent AF over a follow-up of 1 to 5 years (HR, 0.4; 95% CI , 0.24 to 0.69; p<.001) and more than 5 years (HR , 0.23; 95% CI, 0.12 to 0.42; p<.001) for all patients. This study was limited by its retrospective design and lack of propensity score matching.

Subsection Summary: Traditional Maze versus "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 (e.g., 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 2 small RCTs 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 (e.g., 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.

Systematic Reviews
A Cochrane review by Huffman et al (2016) evaluated the evidence on concomitant AF surgery for patients undergoing cardiac surgery.[7,] 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, 3 trials used microwave ablation, 2 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.[8,] Nine studies were selected and analyzed: 5 evaluated RFA, 2 evaluated Cox maze "cut-and-sew," 1 evaluated cryoablation, and 1 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 [OR], 1.45; 95% CI, 0.55 to 3.83; p=.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%; OR , 13.96; 95% CI, 6.29 to 30.99; p<.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.[9,] 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 (e.g., 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).[10,] 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<.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=.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 a RCT that randomized 224 patients from 3 clinical centers to cardiac surgery plus ablation or to cardiac surgery alone.[11,] Patients were eligible for inclusion if they had at least 2 documented episodes of 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 1 year following surgery, and the primary safety outcome was a composite outcome of death, myocardial infarction (MI), stroke, or new-onset renal failure requiring hemodialysis at 30 days post-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) 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 1 year.

Van Breugel et al (2010) evaluated changes in quality of life in a related patient population.[12,] One hundred fifty patients with AF who were scheduled to undergo valve 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).[13,] 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.[14,] 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, 2020) 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.[15,16,17,18,]

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 versus 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:

Populations
The relevant population of interest is individuals with symptomatic drug-resistant AF or flutter not undergoing cardiac surgery with bypass.

Interventions
The therapies being considered are stand-alone minimally invasive, off-pump thoracoscopic maze procedures.

Comparators
The following practice is currently being used to treat individuals with symptomatic drug-resistant AF or flutter not undergoing cardiac surgery with bypass: medical management or catheter ablation (CA).

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.

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

Van Laar et al (2017) reported on a meta-analysis of stand-alone thoracoscopic maze procedures for the treatment of AF.[19,] Reviewers included 14 studies (3 RCTs, 7 prospective cohort studies, 11 observational studies; 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.

Yi et al (2020) conducted a systematic review of 6 RCTs (N=466) comparing thoracoscopic surgical ablation with CA with regard to clinical outcomes in patients with AF.[20,] For the review's primary efficacy outcome of freedom from atrial tachyarrhythmia without antiarrhythmic drug use, treatment success was significantly higher in the surgical ablation group as compared to the CA group (75% vs. 57.1%; OR, 0.41; 95% CI, 0.2 to 0.85; p=.02). However, a significantly increased number of serious adverse events were seen in the surgical versus CA group (OR, 0.16; 95% CI, 0.006 to 0.46; p=.0006).

Phan et al (2016) conducted a systematic review of studies comparing thoracoscopic surgical ablation with CA , including the Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment (FAST) trial.[21,] Eight comparative studies, with a total of 321 video-assisted thoracoscopic surgical ablation patients and 378 CA 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 CA group (64.3%) at 6 months post procedure (RR, 1.23; 95% CI, 1.02 to 1.49; p=.03). This difference was maintained at 12 months post procedure. 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, MI , conversion to complete thoracotomy) compared with CA -treated patients (28.2% vs 7.8%; RR, 3.30; 95% CI, 1.73 to 6.29; p<.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).[22,] 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 CA (Table 3). FAST compared stand-alone surgical ablation with percutaneous ablation.[23,] 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 CA. 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 CA 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 CA group (p=.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 CA group (p<.001). Serious adverse events were more common in the surgical group (23.0% [14/61]) than the CA group (3.2% [2/63]; p=.001). In each group, there was 1 episode of tamponade and stroke. Additional complications in the surgical group included 6 patients with pneumothorax, 2 who required pacemaker insertion, and 1 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.[24,] 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 CA group (56% [34/61] versus 87% [55/63]; adjusted HR, 0.40; 95% CI, 0.25-0.64; p<.001). Additional ablation procedures were more common in the CA group (49% versus 13%; p<.001). Rates of the composite outcome of death, MI, or cerebrovascular event (transient ischemic attack, ischemic or hemorrhagic stroke) were similar between groups (15% following thoracoscopy [9/61] and 16% following CA [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 CA procedure for AF to repeat CA (n=32) or to surgical ablation with video-assisted thoracoscopy (n=32).[25,] 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=.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=.02).

Additionally, Adiyaman et al (2018) published results of a small, single-center RCT 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.[26,] 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% v s 29.2%; HR, 0.56; 95% CI, 0.26-1.20) and major complications were greater in the MIPI group (20.8% in MIPI v s 0% in CA; difference, 20.8%; 95% CI, 4.8%–36.9%; p=.029).

The CASA-AF trial, reported by Haldar et al (2020), is the first RCT that evaluated the efficacy and safety of thoracoscopic surgical ablation versus CA as the index procedure in 120 patients with long-standing persistent AF.[27,] Tables 3 and 4 summarize the key characteristics and results of the CASA-AF trial. Beyond the tabular results, a reduction in AF burden of ≥75% was seen in 67% in the surgical ablation group versus 77% in the CA group (OR, 1.13; 95% CI, 0.67-4.08; p=.3). Improvements in AF symptoms were increased following CA; surgical ablation was more expensive and was associated with fewer quality-adjusted life years (p=.02) compared with CA.

Table 3. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	**Comparator**
Haldar (2020); CASA-AF[27,]	UK	4	2015-2018	Individuals with long-standing PersAF, EHRA symptom score >2 and left ventricular ejection fraction ≥40%	Stand-alone surgical ablation, N=60	CA, N=60
Boersma (2012); FAST[23,]	EU	2	2007-2010	Individuals with symptomatic AF for at least 1 year and had failed at least 1 antiarrhythmic medication; 67% prior failed CA	Stand-alone surgical ablation, N=63	CA , N=63
Pokushalov (2013)[25,]	Russia	1	2011-2013	Individuals with history of symptomatic PAF/PersAF after a previous failed first RF ablation procedure	Stand-alone surgical ablation, N=32	CA , N=32

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
Adiyaman (2018)[26,]	The Netherlands	1	NR	Individuals with symptomatic PAF or early PersAF (continuous AF duration, <3 months) with failure of at least 1 class 1 or 3 antiarrhythmic drugs, but no previous CA	Stand-alone surgical ablation, N=26	CA , N=26

AF: atrial fibrillation; CA: catheter ablation; EHRA: European Heart Rhythm Association; EU: Europe; FAST: Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment; NR: not reported; PAF: paroxysmal atrial fibrillation; PersAF: persistent atrial fibrillation; RCT: randomized controlled trial; RF: radiofrequency; UK: United Kingdom.

Table 4. Summary of Key RCT Results

Study	Freedom from AF while off all antiarrhythmic drugs	Mortality	Serious Adverse Events	Recurrence of atrial arrhythmias
Haldar (2020); CASA-AF[27,]	1-year		1-year	
Surgical ablation	26% (14/54)	1	18% (10/55)	NR
Catheter ablation	28% (17/60)	0	15% (9/60)	NR
Relative measure	OR 1.128, 95% CI, 0.46-2.82, p=.84	NR	p=.65	NR
Boersma (2012); FAST[23,]	1-year	1-year	1-year	7-years
Surgical ablation	65.6% (40/61)	0	23.0% (14/61)	56% (34/61)
Catheter ablation	36.5% (23/63)	1.6% (1/63)	3.2% (2/63)	87% (55/63)
Relative measure	p=.002	NR	p=.001	HR 0.40, 95% CI 0.25-0.64; p<.001)
Pokushalov (2013)[25,]	1-year	1-year	1-year	1-year
Surgical ablation	81% (26/32)	0	7[1]	3% (1/32)
Catheter ablation	47% (15/32)	0	1[1]	9% (3/32)
Relative measure	p=.004	N/A	p=.02	NR
Adiyaman (2018)[26,]	2 years	2 years	2 years	2 years
Surgical ablation	29.2%	0	NR	20.8%
Catheter ablation	56%	0	NR	0%

Study	Freedom from AF while off all antiarrhythmic drugs	Mortality	Serious Adverse Events	Recurrence of atrial arrhythmias
Relative measure	HR 0.56; 95% CI, 0.26–1.20	N/A	NR	Difference, 20.8%; 95% CI, 4.8%–36.9%

[1]Number of events
AF: atrial fibrillation; CI: confidence interval; HR: hazard ratio; N/A: not applicable; NR: not reported; OR: odds ratio; RCT: randomized controlled trial.

Table 5. Study Relevance Limitations of Key RCTs

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Haldar 2020; CASA-AF[27,]	4. Study population included patients at 4 highly specialized centers, which may have an impact on generalizability				
Boersma (2012); FAST[23,]	4. Most patients had undergone a prior unsuccessful catheter ablation and had paroxysmal atrial fibrillation				
Pokushalov (2013)[25,]				4. Not established and validated measures: Used implantable loop recorder to measure atrial fibrillation, which "may detect more episodes than many centers routinely capture using external ECG methods and does not exactly conform to HRS guidelines"	
Adiyaman (2018)[26,]					

ECG: Electrocardiography; HRS: Heart Rhythm Society; RCT: randomized controlled trial.
The study 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.
[c] 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

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Haldar (2020); CASA-AF[27,]		1. Not blinded to treatment assignment; 2. Not blinded outcome assessment				
Boersma (2012); FAST[23,]	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%)	1. Not blinded to treatment assignment; 2. Not blinded outcome assessment				
Pokushalov (2013)[25,]	3. Allocation concealment unclear: "coded envelope system";	1. Not blinded to treatment assignment; 2. Not blinded outcome assessment				

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
	"although not statistically significant, the CA group enrolled more patients with persistent AF" (44% vs 37%)					
Adiyaman (2018)[26,]	3. Allocation concealment unclear; not described	1. Not blinded to treatment assignment; 2. Not blinded outcome assessment				

AF: atrial fibrillation; CA: catheter ablation; 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] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

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 CA (Tables 7 and 8).[28,29,30,] 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 CA (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

Study	Study Type	Country	Dates	Participants	Surgical Ablation Type	Catheter Ablation	Follow-Up	Matching variables
Mahapatra (2011)[28,]	Case series with matched control groups	US	2007-2009	Persistent or LSP AF who have failed ≥ 1 prior CA	Combined epicardial-surgical and endocardial-catheter, N=15	Repeat CA, N=30	20.7 m	LA size by echo, AF duration, AF type, use of post-ablation AAD, lack of prior cardiac surgery, and left ventricular ejection fraction
Stulak (2011)[29,]	Case series with matched control groups	US	1993-2007	Lone AF, 10% with prior CA	Isolated biatrial cut-and sew Cox-Maze III procedure, N=97	CA, N=194	5.6 y for SA; 3.1 y for CA	Median age, age range, male, intermittent AF
Wang (2011)[30,]	Case series with matched control groups	China	2006-2009	Long-standing persistent AF (i.e., continuous AF for ≥ 1 year), resistant to either electrical or pharmacological cardioversion; no previous CA	Video-assisted minimally invasive ablation, N=83	CA, N=83	2.2 y	AF duration, left atrial dimension and sex

AAD: anti-arrhythmic drug; AF: atrial fibrillation; CA: catheter ablation; LA: left atrial; LSP: long-standing persistent; SA: surgical ablation; US: United States.

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

Study	Free of atrial arrhythmia and off of AAD	Freedom from recurrence	Need for repeat ablation	Death	Overall Complications
Mahapatra (2011)[28,]	45	45	45	45	45
SA+CA	86.7% (13/15)	93.3% (14/15)	0	0	0
Repeat CA	53.3% (16/30)	56.7% (17/30)	10% (3/30)	0	3.33% (1/30)
Measure of association	p=.04	p=.01	p=.15	NR	NR
Stulak (2011)[29,]	N=265	N=265	N=265	N=265	N=265
SA	82%	NR	6.5% (6/93)	0	NR
CA	56%	NR	24% (41/172)	0	NR
Measure of association	p<.001		NR		NR
Wang (2011)[30,]	166	166	166	166	
SA	61.4%	NR	6.0% (5/83)	1.2% (1/83)	NR
CA	44.6%	NR	27.7% (23/83)	2.4% (2/83)	NR
Measure of association	p=.043	HR 0.555 (95% CI, 0.354, 0.872)	NR	NR	NR

AAD: anti-arrhythmic drug; CA: catheter ablation; CI: confidence interval; Diff: difference; HR: hazard ratio; NR: not reported; OR: odds ratio; RR: relative risk; SA: surgical ablation.

Other observational studies have reported outcomes for stand-alone AF treatment. 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.[31,] 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=.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.[32,] 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 3 sternotomy or mini-thoracotomy procedures due to complications, 2 cases of late pericardial tamponade, 1 case of pericardial effusion requiring video-assisted thoracoscopic surgery, and 1 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).[33,]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.[34,35,36,37,38,39,40,41,42,43,44,] 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.[44,] 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 CA. 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 CA. For example, Ad et al (2011) reported on 40 patients who had failed CA , with a mean of 2.3 prior ablations per patient.[45,] 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 CA s; 17 with paroxysmal AF, 12 with persistent AF, and 5 with long-standing persistent AF.[46,] 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 4 RCTs (including the FAST study) and many case series, some with matched control groups. The RCTs have had mixed results. Two RCTs reported significantly higher rates of freedom from AF at 1-year with surgical ablation, but also reported significantly higher rates of serious adverse events. The remaining 2 RCTs found no significant differences between treatment groups in rates of freedom from AF and either did not assess or did not find significant differences in serious adverse events. The comparative observational studies consistently found significantly higher rates of freedom from atrial arrhythmias, but lacked assessment of serious adverse events. This evidence does not support the superiority of 1 technique over the other but suggests that other factors (e.g., type of AF, prior treatments, inability to take anticoagulation, patient preference) may influence the decision for the type of procedure. Additionally, the studies do not permit conclusions about harms due to heterogenous measurement across studies, with mixed results. Case series with matched control groups have reported higher success rates in maintaining sinus rhythm compared with CA. 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 versus other treatments.

Some case series and a RCT have included only patients who have failed previous CA. These studies have also reported high success rates following thoracoscopic ablation, suggesting that patients who fail CA may still benefit from thoracoscopic ablation. However, the RCT reported higher adverse event rates than CA , 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:

Populations

The relevant population of interest is individuals with symptomatic drug-resistant AF or flutter not undergoing cardiac surgery with bypass.

Interventions

The therapies being considered are hybrid thoracoscopic and endocardial ablation procedures.

Comparators

The following practice is currently being used to treat individuals with symptomatic drug-resistant AF or flutter not undergoing cardiac surgery with bypass: medical management or catheter ablation (CA).

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.[47,] 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.

Randomized Controlled Trials

DeLurgio et al (2020) evaluated the efficacy and safety of a minimally invasive epicardial/endocardial ablation approach (Hybrid Convergent) as compared to CA in 153 patients with persistent and long-standing persistent AF in the Convergence of Epicardial and Endocardial Ablation for the Treatment of Symptomatic Persistent AF (CONVERGE) trial.[48,] Patients were randomly assigned to Hybrid Convergent (n=102) or CA (n=51) at 27 sites in the United States and United Kingdom. The primary effectiveness endpoint was freedom from AF/atrial flutter/atrial tachycardia absent of class I/II antiarrhythmic drugs through the 12 months post procedure. Secondary efficacy endpoints included AF burden reduction (defined as the proportion of patients achieving at least 90% reduction in AF burden at 12 months when compared with baseline) and AF freedom at 12 months. The primary safety endpoint was the incidence of major adverse events which included cardiac tamponade; severe pulmonary vein stenosis; excessive bleeding; MI, stroke, transient ischemic attack, atrioesophageal fistula, phrenic nerve injury, and death. No deaths, cardiac perforations, or atrioesophageal fistulas occurred in the trial. The safety rate was primarily driven by inflammatory pericardial effusions observed between 1 and 3 weeks post procedure in the Hybrid Convergent arm; best practices for management of this adverse event such as adequate drain management, anti-inflammatory prophylaxis, and improved patient monitoring should be implemented. Tables 9 and 10 present a summary of the key characteristics and main results of the CONVERGENT trial. Study relevance, design, and conduct limitations are presented in Tables 11 and 12.

Table 9. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
DeLurgio (2020); CONVERGE[48,]	US; UK	27	Dec 2013-Aug 2018	Adults with symptomatic persistent AF refractory or intolerant to at least 1 class I/II antiarrhythmic drug and a left atrium size of ≤6 cm	Hybrid Convergent, n=102	CA, n=51

AF: atrial fibrillation; CA: catheter ablation; RCT: randomized controlled trial; UK: United Kingdom; US: United States.

Table 10. Summary of Key RCT Results

Study	Freedom from AF/atrial flutter/atrial tachycardia absent of class I/II antiarrhythmic drugs	AF burden reduction	AF freedom	Major adverse events
DeLurgio (2020); CONVERGE[48,]	1-year	1-year	1-year	Between 8- and 30-days post procedure
Hybrid Convergent	67.7% (67/99)	80% (60/75)	71% (72/102)	7.8% (8/102)
Catheter ablation	50% (25/50)	56.8% (25/44)	51% (26/51)	0%
Success rate difference (%)	17.7 (RR, 1.35; p=.036)	23.2% (RR, 1.41; p=.007)	20% (RR, 1.39; p=.0172)	p=.0525

AF: atrial fibrillation; RCT: randomized controlled trial; RR: risk ratio.

Table 11. Study Relevance Limitations of Key RCTs

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
DeLurgio (2020); CONVERGE[48,]			2. Absence of empirical endocardial posterior wall ablation in the CA group	1. Major adverse events were only reported through 30 days and not through the 12-month follow-up	

CA: catheter ablation; RCT: randomized controlled trial.
The study 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.
[c] 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 12. Study Design and Conduct Limitations of Key RCTs

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
DeLurgio (2020); CONVERGE[48,]	3. Allocation concealment was not described in the publication or the protocol.	1. Subjects and clinicians not blinded to treatment assignment				

RCT: randomized controlled trial.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

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.[49,] 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=.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=.001). Significantly more patients in the hybrid group were on warfarin at 1 year (29% vs 13.4%, p<.001). There was no difference between groups on the frequency of adverse events.

Kress et al (2017) evaluated clinical outcomes in 133 patients with persistent and long-standing AF who underwent conventional endocardial ablation (only RFA; n=69) or a hybrid approach of endocardial CA and epicardial ablation (n=64).[50,] Results revealed that the hybrid approach was associated with less recurrence (37% vs. 58%; p=.013) and repeat ablation (9% vs. 26%, p=.012) as well as an improvement in AF-free survival (72% vs. 51%; p=.01). Although the hybrid intervention was associated with a longer length of stay (p<.001), the occurrence of 30-day periprocedural complications was similar between the groups (p=.205). Complications were evaluated based on the Heart Rhythm/European Heart Rhythm Association/European Cardiac Arrhythmia Society/Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología consensus guidelines and included pericardial infusion, groin complications, cerebrovascular accident, and death. There were a total of 7 complications overall (5.3%): 5 (7.8%) in the hybrid group and 2 (2.9%) in the endocardial group

Maclean et al (2020) compared the efficacy and safety of a hybrid convergent procedure (surgical AF ablation combined with CA) in 43 patients with longstanding persistent AF with a matched group of 43 patients who underwent CA alone.[51,] At 1 year, patients who had undergone the hybrid convergent procedure had an increased AF-free survival on (60.5% vs. 25.6%; p=.002) and off (37.2% vs. 13.9%; p=.025) antiarrhythmic drugs as compared to the CA group. Additionally, after 30.5 ± 13.3 months of follow-up, increased arrhythmia-free survival was significantly improved in the convergent, as compared to the CA group, both on (58.1% vs. 30.2%; p=.016) and off (32.5% vs. 11.6%; p=.036) antiarrhythmics. Complications were reported more frequently in the convergent group (11.6% vs. 2.3%; p=.2). Serious adverse events related to the epicardial procedure included an inferior vena cava rupture requiring emergency sternotomy (n=1) and a pericardial hernia requiring surgical correction 6 months postoperatively (n=1). During CA, tamponade requiring emergency pericardiocentesis occurred in 2 patients in the hybrid convergent group versus 1 patient in the CA alone group. Phrenic nerve palsy was also reported in 1 patient in the convergent group following CA.

Observational Studies

Other relevant single-arm case series have included populations ranging from 19 to 104 patients.[52,53,54,55,56,57,58,59,60,61,62,] 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 single RCT (CONVERGENT) and nonrandomized comparative studies that compare a hybrid procedure to a standard percutaneous procedure, a number of single-arm case series, and a systematic review of these studies. Results of the CONVERGENT RCT and nonrandomized comparative studies have generally found an increased rate of AF-free survival with use of a hybrid procedure as compared to CA in patients with persistent and long-standing AF. However, risk of harm is not well characterized. Data regarding serious adverse events for at least 1 year following procedure were not reported in the available RCT. Observational studies suggest higher adverse events with hybrid approaches.

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 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 an 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.

Two RCTs reported significantly higher rates of freedom from AF at 1-year with surgical ablation, but also reported significantly higher rates of serious adverse events. The remaining 2 RCTs found no significant differences between treatment groups in rates of freedom from AF and either did not assess or did not find significant differences in serious adverse events. The comparative observational studies consistently found significantly higher rates of freedom from atrial arrhythmias, but lacked assessment of serious adverse events. The noncomparative studies 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. Additionally, the studies do not permit conclusions about harms due to heterogenous measurement across studies, with mixed results. The evidence is insufficient to determine that the technology results in an 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 hybrid thoracoscopic and endocardial ablation procedures, the evidence includes an RCT by DeLurgio et al [2020], and 2 observational studies (Kress et al [2017] and Maclean et al [2020], N=372) that compared a 'convergent' hybrid approach (i.e., epicardial approach combined with endocardial ablation to catheter ablation) and 1 observational study that compared a thoracoscopic epicardial ablation with a percutaneous trans-septal procedure hybrid approach to catheter ablation (LeMeir et al, 2012, n=63). The DeLurgio (2020) RCT (n=153) found a statistically significantly higher rate on the primary outcome of freedom from AF/atrial flutter/atrial tachycardia absent of class I/II antiarrhythmic drugs at 1-year, but with a nonstatistically significantly higher rate of major adverse events (p=.0525) between 8- and 30-days post procedure. Major adverse events were not reported for the 1-year follow-up period. The 2 observational studies of the convergent hybrid approach found that it was associated with an increased rate of AF-free survival, but major adverse events at 1-year were nonsignificantly more common. LeMeir et al (2012) found that the thoracoscopic epicardial ablation with a percutaneous trans-septal procedure hybrid approach was associated with an increased rate of AF-free survival and no difference in adverse events. For the 'convergent' hybrid approach, additional multicenter RCTs are needed with comparisons to catheter ablation that measure the freedom from AF and assess adverse events after at least 1-year of follow-up. For other types of hybrid approaches, multicenter RCTs are needed that use established techniques to control for bias and assess both benefits and harms with at least 1-year of follow-up. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

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 (e.g., 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 (e.g., 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

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

Society of Thoracic Surgeons

In 2017, the Society of Thoracic Surgeons published guidelines on the surgical treatment of atrial fibrillation (AF).[63,] Recommendations are provided in Table 13.

Table 13. Guidelines on Surgical Treatment of Atrial Fibrillation

Recommendation	COR	LOE
Surgical ablation for AF is recommended at the time of concomitant mitral operations to restore sinus rhythm.	I	A
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.	I	B
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.	IIa	B

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

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.[64,] Recommendations on the use of surgical ablation to maintain sinus rhythm are provided in Table 14.

Table 14. Guidelines on the Management of Atrial Fibrillation

Recommendation	COR	LOE
"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)."	IIb	B-R

AF: atrial fibrillation; COR: class of recommendation; HF: heart failure; LOE: level of evidence.
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.[65,] The statement was endorsed by 4 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 15.

Table 15. Guidelines on Concomitant Surgical Ablation in Patients Undergoing Cardiac Surgery[a]

Recommendation	COR	LOE
Paroxysmal: Surgical ablation is recommended for patients undergoing surgery for other indications	II	B-NR
Persistent: Surgical ablation is recommended for patients undergoing surgery for other indications	II	B-NR
Longstanding Persistent: Surgical ablation is recommended for patients undergoing surgery for other indications	II	NR

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

The following recommendations were made on stand-alone and hybrid surgical ablation in patients with symptomatic AF refractory or intolerant to at least one class 1 or 3 antiarrhythmic medication (Table 16).

Table 16. Guidelines on Stand-Alone and Hybrid Surgical Ablation for Symptomatic Atrial Fibrillation Refractory or Intolerant to Antiarrhythmics

Recommendation[a]	COR	LOE
Paroxysmal		
Stand alone surgical ablation can be considered for patients who have not failed catheter ablation but prefer a surgical approach	IIb	B-NR
Stand alone surgical ablation can be considered for patients who have failed one or more attempts at catheter ablation	IIb	B-NR
Persistent		
Stand alone surgical ablation is reasonable for patients who have not failed catheter ablation but prefer a surgical approach	IIa	B-NR
Stand alone surgical ablation is reasonable for patients who have failed one or more attempts at catheter ablation	IIa	B-NR

Recommendation[a]	COR	LOE
Longstanding persistent		
Stand alone surgical ablation is reasonable for patients who have not failed catheter ablation but prefer a surgical approach	IIb	B-NR
Stand alone surgical ablation is reasonable for patients who have failed one or more attempts at catheter ablation	IIb	B-NR

COR: class of recommendation; LOE: level of evidence ; 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.[66,] Recommendations on concomitant surgical ablation in patients with AF are provided in Table 17.

Table 17. Guidelines on Concomitant Surgical Ablation in Patients with Atrial Fibrillation

Recommendation	COR	LOE
"Addition of a concomitant surgical ablation procedure for AF does not increase the incidence of perioperative morbidity."	IIa	A, B-R, B-NR[a]
"Addition of a concomitant surgical ablation procedure for AF does not change the incidence of perioperative stroke/TIA."	IIa	A
"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-NR[b]
"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-NR[c]

AF: atrial fibrillation; COR: class of recommendation; HRQL: health-related quality of life; LOE: level of evidence ; 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)."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 18.

Table 18. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04237389	Comparative Assessment of Catheter and Thoracoscopic Approaches in Patients With Persistent and Long-standing Persistent Atrial Fibrillation	60	Aug 2022
NCT03546374	Irrigated Radio Frequency Ablation to Terminate Non-Paroxysmal Atrial Fibrillation (Terminate AF Study)	160	May 2022
NCT03732794	AtriCure CryoICE Lesions for Persistent and Long-standing Persistent Atrial Fibrillation Treatment During Concomitant On-Pump Endo/Epicardial Cardiac Surgery	150	Jul 2024
NCT02393885	Pivotal Study Of A Dual Epicardial & Endocardial Procedure (DEEP) Approach for Treatment of Subjects With Persistent or Long Standing Persistent Atrial Fibrillation With Radiofrequency Ablation	220	Dec 2026
NCT04715425	Thoracoscopic Surgical Versus Catheter Ablation Approaches for Primary Treatment of Persistent Atrial Fibrillation	170	Sep 2028
Unpublished			
NCT02047279	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	120	Sep 2017 (completed)
NCT02441738	Hybrid Thoracoscopic Surgical and Transvenous Catheter Ablation Versus Transvenous Catheter Ablation in Persistent and Longstanding Persistent Atrial Fibrillation	41	Dec 2018 (completed)

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

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS

33254	Operative tissue ablation and reconstruction of atria, limited (e.g., modified maze procedure)
33255	Operative tissue ablation and reconstruction of atria, extensive (eg, maze procedure); without cardiopulmonary bypass
33256	Operative tissue ablation and reconstruction of atria, extensive (eg, maze procedure); with cardiopulmonary bypass
33257	Operative tissue ablation and reconstruction of atria, performed at the time of other cardiac procedure(s), limited (e.g., modified maze procedure) (List separately in addition to code for primary procedure)
33258	Operative tissue ablation and reconstruction of atria, performed at the time of other cardiac procedure(s), extensive (eg, maze procedure), without cardiopulmonary bypass (List separately in addition to code for primary procedure)
33259	Operative tissue ablation and reconstruction of atria, performed at the time of other cardiac procedure(s), extensive (eg, maze procedure), with cardiopulmonary bypass (List separately in addition to code for primary procedure)
33265	Endoscopy, surgical; operative tissue ablation and reconstruction of atria, limited (e.g., modified maze procedure), without cardiopulmonary bypass
33266	Endoscopy, surgical; operative tissue ablation and reconstruction of atria, extensive (eg, maze procedure), without cardiopulmonary bypass

ICD-10 Diagnoses

I48.0	Paroxysmal atrial fibrillation
I48.11	Longstanding persistent atrial fibrillation
I48.19	Other persistent atrial fibrillation

REVISIONS

08-08-2018	Policy added to the bcbsks.com web site on July 9, 2018, with an effective date of August 8, 2018.
06-19-2019	Updated Description section.
	Updated Rationale section.
	Updated References section.
10-01-2019	In Coding section: ▪ Deleted ICD-10 code: I48.1 ▪ Added ICD-10 codes: I48.11, I48.19
05-05-2021	Updated Description section.
	Updated Rationale section.
	Updated References section.
07-02-2021	Updated Description section.
	Updated Rationale section.
	Updated References section.

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