Medical Policy

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

Related Policies:	▪ *Catheter Ablation as Treatment for Atrial Fibrillation* ▪ *Percutaneous Left Atrial Appendage Closure Devices for Stroke Prevention in Atrial Fibrillation*

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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:	Interventions of interest are:	Comparators of interest are:	Relevant outcomes include:

Populations	Interventions	Comparators	Outcomes
• With symptomatic, drug-resistant atrial fibrillation or flutter who are not undergoing cardiac surgery with bypass	• Minimally invasive, off-pump thoracoscopic maze procedures	• Medical management • Catheter ablation	• 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.

Epidemiology

In the US, more than 3 to 6 million people have AF and it has been estimated that more than 12 million people will have AF by 2030.[1,2,3,] Age, body mass index, height, hypertension, diabetes mellitus, obstructive sleep apnea, myocardial infarction, heart failure, hyperthyroidism, chronic kidney disease, smoking, moderate to heavy alcohol consumption, and genetic predisposition are all risk factors for AF.[4,3,] Age-adjusted AF incidence and prevalence is higher among men than women, although the lifetime risk is similar at 24% for men and 22% for women[5,]. AF incidence and prevalence appear lower in individuals who are Black compared to White, despite a higher

burden of comorbidities. However, this difference is likely largely explained by differential detection of AF by race/ethnicity.[6,]

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 (CA) 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 CA.

Regulatory Status

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

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

Device	Manufacturer
EPi-Sense Guided Coagulation System	Atricure
Medtronic DiamondTemp™ System	Medtronic
Cobra Fusion Ablation System	AtriCure
Medtronic Cardioblate® and Cardioblate Gemini™ Systems	Medtronic
Cardima Ablation System	Cardima
Epicor™ Medical Ablation System	Epicor Medical
Isolator™ Systems	AtriCure
Estech COBRA® Cardiac Electrosurgical Unit	Endoscopic Technologies
Coolrail™ Linear Pen	AtriCure
Numeris® Guided Coagulation System with VisiTrax®	nContact Surgical
EPi-Sense® Guided Coagulation System with VisiTrax®	nContact Surgical

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 or Cleared by the U.S. Food and Drug Administration

Device	Manufacturer
Cryocare® Cardiac Surgery System	Endocare
SeedNet™ System	Galil Medical
SurgiFrost® XL Surgical CryoAblation System	CryoCath Technologies; now Medtronic
Isis™ cryosurgical unit	Galil Medical
Artic Front Advance™ and Arctic Front Advance Pro™ and the Freezor Max™ Cardiac Cryoablation Catheters	Medtronic

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 the treatment of symptomatic atrial fibrillation or flutter.

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

POLICY GUIDELINES

A. Given the availability of less-invasive alternative approaches to treat atrial fibrillation, performing the maze procedure without concomitant cardiac surgery should rarely be needed.

B. 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.

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.

RATIONALE

This evidence review was created with searches of the PubMed database. The most recent literature update was performed through November 19, 2024.

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 AS AN ADJUNCT TO OPEN HEART SURGERY

Clinical Context and Therapy Purpose

The purpose of maze and related procedures in addition to on-bypass surgeries in individuals who have atrial fibrillation (AF) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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.

Atrial fibrillation can be subdivided into 3 types: paroxysmal, persistent, and permanent. Paroxysmal AF episodes last <7 days and are self-terminating. Persistent AF episodes last for >7 days and are not self-terminating; long-standing persistent AF is persistent AF that lasts for more than a year. In permanent AF, normal rhythm cannot be restored. Individuals with paroxysmal AF may progress to persistent or permanent AF over time.

Interventions

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

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 the 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.

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). The success rate of CA remains low for long-standing persistent AF.

Outcomes

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

The 2017 joint expert consensus statement (including Heart Rhythm Society) on catheter and surgical ablation of AF affirmed that freedom from any atrial arrhythmia, defined as AF, atrial flutter, or atrial tachycardia, lasting for more than 30 seconds off antiarrhythmic drug therapy, is the gold standard for reporting the efficacy of ablation in AF trials. The statement also suggests that there should be a minimum of 12 months follow-up.[7,]

Many patients have asymptomatic AF episodes after ablation. Therefore, monitoring for symptoms alone is not sufficient to measure freedom from AF. AF monitoring can be performed with noncontinuous or continuous monitoring tools. Noncontinuous tools include electrocardiograms (ECGs), Holter devices, patient- and automatically activated devices, and external loop recorders. Continuous monitoring tools include implantable pacemakers or defibrillators and implantable loop recorders. [7,]

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

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.

Systematic Reviews

Sakurai et al (2025) reported long-term survival outcomes from a systematic review and meta-analysis of 38 studies (n=41,678) comparing surgical ablation with no surgical ablation during cardiac surgery.[8,] The analysis included 9 RCTs and 15 comparative observational studies. The median follow-up was 62 months. Surgical ablation was associated with decreased risk of

mortality (HR=0.78; 95% CI, 0.71 to 0.84), stroke (HR=0.60; 95% CI, 0.48 to 0.76), heart failure rehospitalization (HR=0.92; 95% CI, 0.87 to 0.96) and freedom from AF (RR=1.93; 95% CI, 1.50 to 2.49). Surgical ablation was also associated with higher risk of permanent pacemaker implantation (HR=1.35; 95% CI, 1.03 to 1.77).

A Cochrane review by Huffman et al (2016) evaluated the evidence on concomitant AF surgery for patients undergoing cardiac surgery.[9,] 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 radiofrequency ablation (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% confidence interval [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.[10,] 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 the 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 in 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.

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).[11,] 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.[12,] 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 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 1 year.

Van Breugel et al (2010) evaluated changes in quality of life in a related patient population.[13,] 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.

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. 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 have reported success rates of the procedure in different populations, with rates of freedom from AF ranging from 53% to 79% at the latest follow-up.[15,16,17,18,19,]

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 individuals who have AF is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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. This section focuses on thoracoscopic maze procedures. Hybrid approaches include concomitant epicardial and endocardial procedures and are discussed separately.

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.

Less invasive, transthoracic, endoscopic, and 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.

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 CA. The success rate of CA remains low for long-standing persistent AF.

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

The 2017 joint expert consensus statement (including Heart Rhythm Society) on catheter and surgical ablation of AF affirmed that freedom from any atrial arrhythmia, defined as AF, atrial flutter, or atrial tachycardia, lasting for more than 30 seconds off antiarrhythmic drug therapy, is the gold standard for reporting the efficacy of ablation in AF trials. The statement also suggests that there should be a minimum of 12 months follow-up.[7,]

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.

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.[20,] 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, 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.[21,] 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.[22,] 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 postprocedure (RR, 1.23; 95% CI, 1.02 to 1.49; p=.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, 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).

Randomized Controlled Trials

Tables 3 and 4 outline characteristics and results of key RCTs; tables 5 and 6 outline limitations related to their relevance, design, and conduct. The Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment (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 hazard ratio [HR] , 0.40; 95% CI, 0.25 to 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 to 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% vs 29.2%; HR, 0.56; 95% CI, 0.26 to 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% to 36.9%; p=.029).

The Catheter Ablation Versus Thoracoscopic Surgical Ablation in Long Standing Persistent Atrial Fibrillation (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 to 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. Long-term (up to 3 years) outcomes of the CASA-AF trial were reported by Boyalla et al (2024).[28,] 104 participants (90%) completed 36-month follow-up (CA, n=57 vs SA, n=47). 7 participants (12%) in the CA group and 5 (11%) in the surgical ablation group were free from atrial fibrillation/tachycardia (AF/AT)≥30 seconds at 36 months (HR=1.2; 95% CI, 0.81 to 1.83; p=.41]. 33 patients (58%) in the CA group versus 26 (55%) in the surgical ablation group had their AF/AT burden reduced by ≥75% (HR=1.04; 95% CI, 0.57 to 1.88; p=.91). The mean quality-adjusted life years, calculated as the area under the EuroQol 5 Dimension 5 Level questionnaire index score, were 2.5 (95% CI, 2.3 to 2.6) for CA versus 2.3 (95% CI, 2.1 to 2.5) for surgical ablation.

Table 3. Summary of Key RCT Characteristics

Study	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	Stand-alone surgical ablation, N=63	CA, N=63

Study	Countries	Sites	Dates	Participants	Interventions	
				antiarrhythmic medication; 67% prior failed CA		
Pokushalov (2013)[25,]	Russia	1	2011-2013	Individuals with a history of symptomatic PAF/PersAF after a previous failed first RF ablation procedure	Stand-alone surgical ablation, N=32	CA, N=32
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; 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
CA	28% (17/60)	0	15% (9/60)	NR
Relative measure	OR, 1.128; 95% CI, 0.46 to 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)

Study	Freedom from AF while off all antiarrhythmic drugs	Mortality	Serious Adverse Events	Recurrence of atrial arrhythmias
CA	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 to 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)
CA	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%
CA	56%	0	NR	0%
Relative measure	HR, 0.56; 95% CI, 0.26 to 1.20	N/A	NR	Difference, 20.8%; 95% CI, 4.8% to 36.9%

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

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 CA and had paroxysmal AF				
Pokushalov (2013)[25,]				4. Used implantable loop recorder to	

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
				measure AF, 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,]					

AF: atrial fibrillation;CA: catheter ablation; 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. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

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	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]
	score and more prior failed ablation (74% vs 63%) and had fewer males (74% vs 87%)					
Pokushalov (2013)[25,]	3. Allocation concealment unclear: "coded envelope system"; "although not statistically significant, the CA group enrolled more patients with persistent AF" (44% vs 37%)	1. Not blinded to treatment assignment; 2. Not blinded outcome assessment	1. Not registered until study completion			
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; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[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); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[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; 5. Other

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).[29,30,31,32,] 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 (range 1.5 years to 5.5 years). All studies consistently found higher success rates with surgical ablation.

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)[30,]	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)[31,]	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)[32,]	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)[30,]	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)[31,]	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)[32,]	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 to 0.872)	NR	NR	NR

AAD: anti-arrhythmic drug; CA: catheter ablation; CI: confidence interval; HR: hazard ratio; NR: not reported; SA: surgical ablation.

Other observational studies have reported outcomes for stand-alone AF treatment. Kwon et al (2021) reported a case series of 353 patients with paroxysmal or persistent AF who underwent RFA (n=125), cryoablation (n=97), or totally thoracoscopic surgical ablation (n=131).[29,] Unlike the studies described in Tables 7 and 8, this study did not include matched controls. Patients who underwent thoracoscopic ablation were more likely to have a history of stroke or TIA (p<.001), persistent (as opposed to paroxysmal) AF (p<.001), and enlarged left atrium (p<.001) based on diameter and volume when compared with the CA groups. At 12-month follow-up, similar proportions of patients were free from AF in the RFA (84%), cryoablation (74%), and thoracoscopic ablation groups (85%; p=.07). After controlling for demographic and clinical characteristics, RFA (HR, 1.33; 95% CI, 0.72 to 2.30) and cryoablation (HR, 1.77; 95% CI, 1.03 to 3.06) were associated with an increased risk of AF recurrence relative to thoracoscopic ablation, though the difference was not statistically significant for RFA. Procedural complications occurred in 2% to 4% of patients across treatment groups with no difference among treatments (p=.74).

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.[33,] 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.[34,] 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).[35,]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.[36,37,38,39,40,41,42,43,44,45,46,] Most series lacked a control group, generally only reported short-term outcomes, and did not consistently report adverse events. Vos et al (2020) reported on outcomes for 82 consecutive patients that underwent totally thoracoscopic ablation including left appendage closure.[46,]After a mean follow-up of 4.0 years, 60% of patients were free from atrial arrhythmia; long-term complications were not studied. Harlaar et al (2022) reported long-term outcomes for a consecutive series of 77 individuals with symptomatic long-standing persistent AF.[47,] At 5 years, freedom from AF was 50% in those who had a single thoracoscopic procedure and 68% in those who had a thoracoscopic procedure and also had an endocardial touch-up procedure. Only short-term, procedure-related complications were described.

Several single-arm case series of minimally invasive epicardial ablation have been reported in patients who had failed CA. Ad et al (2011) reported on 40 patients who had failed CA, with a mean of 2.3 prior ablations per patient.[48,] 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 CAs; 17 with paroxysmal AF, 12 with persistent AF, and 5 with long-standing persistent AF.[49,] 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. MacGregor et al (2022) reported long-term outcomes of 236 individuals who underwent a stand-alone Cox-Maze IV procedure (via sternotomy or a minimally invasive approach) for refractory AF.[50,] Median follow-up was approximately 5 years and maximum follow-up was 10 years; 59% of participants had failed a previous CA. Freedom from AF was 94% (187/199), 89% (81/91), and 77% (24/31) at 1, 5, and 10 years, respectively.

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 (samples sizes ranging from 52 to 126), 3 observational studies (samples sizes ranging from 45 to 291), 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 (eg, 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 harm due to heterogeneous 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 does 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.

Additional multicenter RCTs are needed that compare stand-alone minimally invasive, off-pump thoracoscopic maze procedures to catheter ablation that use established techniques to control for bias, adhere to recommended reporting of harms, and clearly define the population for whom the technology is intended.

HYBRID THORACOSCOPIC AND ENDOCARDIAL ABLATION PROCEDURES

Clinical Context and Therapy Purpose

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

"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 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. Hybrid techniques are of particular interest in individuals with persistent and long-standing persistent AF.

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

The hybrid approach first involves surgical epicardial ablation. The epicardial portion of the hybrid approach can be performed thoracoscopically or endoscopically through a subxiphoid incision. The procedure is called 'hybrid convergent' when utilizing endoscopic subxyphoid access. The surgical epicardial portion generally includes 3 main types of lesion sets: posterior box, pulmonary vein isolation (PVI) with connecting roof and floor lines, and posterior left atrial ablation, although the lesion sets have varied.[51,]

Following the epicardial procedure, an electrophysiologic study is performed percutaneously followed by endocardial ablation as directed by the results of electrophysiology. The endocardial ablation offers the opportunity to check line block, confirm PVI, and perform cavotricuspid isthmus ablation. The electrophysiology study and endocardial ablation can be done immediately after the thoracoscopy as part of a single procedure or on separate days, as directed by the electrophysiology study.

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 CA.

The success rate of CA remains low for long-standing persistent AF. Winkle et al (2023) reported on very long-term AF outcomes following CA including 5200 patients undergoing 7145 ablation procedures.[52,] For the initial ablation, freedom from AF at 5, 10, and 15 years was: 68%, 56%, 48% for paroxysmal AF; 47%, 36%, 27% for persistent AF; and 30%, 18%, 3% for long-standing AF. For patients who underwent multiple ablations, freedom from AF following the final ablation at 5, 10, and 15 years was: 80%, 73%, 63% for paroxysmal AF; 60%, 50%, 43% for persistent AF; and 43%, 32%, 21% for long-standing AF.

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

The 2017 joint expert consensus statement (including Heart Rhythm Society) on catheter and surgical ablation of AF affirmed that freedom from any atrial arrhythmia, defined as AF, atrial flutter, or atrial tachycardia, lasting for more than 30 seconds off antiarrhythmic drug therapy, is the gold standard for reporting the efficacy of ablation in AF trials. The statement also suggests that there should be a minimum of 12 months follow-up.[7,]

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

Eranki et al (2023) reported results of a systematic review of mid-term (at least 2 year) outcomes of hybrid ablation.[53,] The review included 1242 individuals from 15 retrospective cohort studies and 1 RCT (Jan, et al, 2018) with sample sizes ranging from 24 to 451. Mean follow-up was 32 (SD=8) months. The mean age of patients was 62 (SD=10) years. 73% of patients were men. 5 studies included patients with paroxysmal AF; the majority of the studies included patients with persistent and long-standing AF. Overall, the mid-term freedom from AF was 75% (95% CI, 67 to 82). Freedom from AF at years 1, 2 and 3 was 78%, 74% and 74%, respectively. There were 12 deaths (0.97%) overall following the hybrid procedure; 10 occurred within 30 days of the procedure. 4 deaths were due to a direct mechanical complication of the procedure (atrio-esophageal fistulae) and 2 patients died of stroke. The pooled complication rate was 5.5% (95% CI, 3 to 9).

Mhanna et al (2021) conducted a systematic review and meta-analysis of 8 controlled studies (including the DeLurgio 2020 RCT and the Kress 2016 and Maclean 2020 nonrandomized studies, discussed below) of 797 patients with AF undergoing hybrid epicardial/endocardial (convergent) ablation (n=366) or standard endocardial ablation (n=431) (Table 9).[54,] Across the studies, the mean age of study participants was 61 years, 77% were male, 93% had persistent AF, and 18% had undergone a previous ablation. The included studies were all assessed as having low to moderate risk of bias. Based on pooled analyses, hybrid ablation was associated with greater freedom from atrial arrhythmia, but also an increased risk of adverse events that included bleeding, pericardial effusion, and cardiac tamponade (Table 10). The study authors noted that across studies 5 deaths were reported among hybrid ablation patients while no endocardial ablation patients died, but no risk estimate was reported.

Eranki et al (2022) conducted a systematic review and meta-analysis of 4 RCTs and propensity score-matched studies (N=422) of hybrid convergent ablation.[55,] All of the included studies are described in more detail in the following sections. Hybrid convergent participants had significantly higher rates of freedom from AF than endocardial ablation participants (OR=2.8; 95% CI, 1.8 to 4.2; p<.01). Major post-operative complications were also significantly higher in hybrid convergent participants (OR=5.1; 95% CI; 1.7 to 15.5; p<.01). One death was reported in the hybrid convergent participants; no deaths were reported in the in the endocardial ablation participants.

Table 9. SR & M-A Characteristics

Study	Dates	Studies	Participants	N (Range)	Design	Duration
Eranki et al (2023)[53,]	2000-2022	16	Patients with AF undergoing hybrid ablation with at least 2 years of follow-up	1242 (24 to 451)	RCTs or observational studies	At least 2 years
Mhanna et al (2021)[54,]	2011-2020	8	Patients with AF undergoing hybrid convergent ablation or standard endocardial ablation	797 (45-222)	RCTs or controlled observational studies	16 to 30 months
Eranki et al (2022)[55,]	Through 2022	4	Patients with AF undergoing hybrid convergent ablation or standard endocardial ablation	422 (50-153)	RCTs or propensity score-matched studies	NR

AF: atrial fibrillation; MA: meta-analysis; NR: not reported; RCT: randomized controlled trial; SR: systematic review;

Table 10. SR & M-A Results

Study	Freedom from Atrial Arrhythmia	Periprocedural Adverse Events[a]	Length of Hospital Stay
Eranki et al (2023)[53,]	At mean of 32 months follow-up	Post-procedural events as defined by the study	NA (reported mid-term events)
Total N	1242	1242	
Pooled effect (95% CI)	75% (67 to 82)	5.5% (3 to 9)	
I^2	83%	71%	
Mhanna et al (2021[54,]			
Total N	N=789 (8 studies)	N=797 (8 studies)	N=355 (3 studies)
Pooled effect (95% CI)	RR 1.48; 95% CI 1.13 to 1.94	RR, 3.64 (95% CI, 2.06 to 6.43)	MD, 3.91 (95% CI, 1.68 to 6.14)
I^2	77%	0%	99%
Eranki et al (2022)[55,]			NR
Total N	N=418 (4 studies)	N=417 (4 studies)	
Pooled effect (95% CI)	OR 2.78; 95% CI 1.82 to 4.24	OR 5.14; 95% CI 1.70 to 15.54	
I^2	0%	0%	

CI: confidence interval; MD: mean difference; NR: not reported; OR: odds ratio; RR: risk ratio.
[a] The most common periprocedural adverse events were bleeding, pericardial effusion, and cardiac tamponade

Randomized Controlled Trials

DeLurgio et al (2020) evaluated the efficacy and safety of a minimally invasive epicardial/endocardial ablation approach with pericardial access achieved via a transdiaphragmatic or subxiphoid incision (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; NCT01984346) trial.[56,] 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 postprocedure 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. Race/ethnicity of participants was not reported in the primary publication but was reported in the registration on ClinicalTrials.gov. Tables 11 and 12 present a summary of the key characteristics and main results of the CONVERGE trial. Study relevance, design, and conduct limitations are presented in Tables 13 and 14.

Lee et al (2022) reported results of the Epicardial Approach in Recurred Atrial Fibrillation (EPIREAF; NCT02979847) RCT comparing a combined epicardial and endocardial ablation approach (n=50) with a conventional endocardial ablation approach (n=50).[57,] In the combined approach, subxiphoid epicardial access was obtained under fluoroscopic guidance (hybrid convergent). Participants had symptomatic, persistent AF refractory or intolerant to antiarrhythmic drugs and prior endocardial ablation. EPIREAF was a single-center, open-label, unblinded trial enrolling participants from June 2016 to November 2019. Rhythm monitoring occurred via 12-lead ECG and 24 hour Holter monitoring at 1, 3, 6, 9, and 12 months after the procedure and then every 6 months thereafter. The primary efficacy outcome was time to recurrence of sustained (>30 seconds) AF or atrial tachycardia following the 90-day blanking period within 12 months of the procedure. The reported safety outcome was occurrence of procedure-related complications within 24 hours after the procedure. Complications included death, any event requiring emergent surgery, severe bradycardia requiring cardiac pacing, pericardial effusion with tamponade or requiring transfusion, ischemic stroke, and procedure-related hematoma or vessel injury. The median age of participants was 59 years and 16% were women. Race/ethnicity of participants was not reported. The median CHA2DS2-VASc score was 1 and the median number of prior ablations was 1. The median procedure time was 232.5 minutes in the hybrid convergent group and 226 minutes in the CA group. Tables 11 and 12 present a summary of the key characteristics and main results of the EPIREAF trial. Study relevance, design, and conduct limitations are presented in Tables 13 and 14.

van der Heijden et al (2023) reported results of the Hybrid Versus Catheter Ablation in Persistent AF (HARTCAP-AF; NCT02441738) RCT[58,]. HARTCAP-AF was a single-center, open-label, unblinded trial randomizing 41 ablation-naive adults with symptomatic, long-standing persistent AF to either hybrid ablation (n=19) or CA (n=22) between October 2016 and December 2018. All randomized participants received their allocated treatment. The hybrid ablation was performed by an experienced surgeon and electrophysiologist in a single-stage procedure. Rhythm observation was performed with a 12-lead ECG and 24-hour-Holter monitor at 3 and 6 months or following

report of symptoms. A 7-day-Holter was collected at 12 months. The primary efficacy outcome was freedom from any atrial tachyarrhythmia (lasting >5 minutes) off antiarrhythmic drugs after the 3-month blanking period until 12 months. The primary safety outcome was a composite of major adverse events and complications occurring within 12 months of follow-up. Major adverse event included death, stroke, bleeding requiring transfusion and/or reoperation, cardiac tamponade or pericardial effusion requiring intervention, empyema, myocardial infarction, pericarditis requiring pericardiocentesis or (prolongation of) (re)hospitalization, pneumothorax requiring intervention (after removal of chest tubes), gastroparesis, symptomatic pulmonary vein stenosis >70%, or (persistent) diaphragmatic paresis. The median age of participants was approximately 65 years; approximately 90% of participants had persistent but not long-standing AF and approximately 10% had persistent, long-standing AF. Several baseline characteristics were not balanced between the 2 treatment groups: women (5% in hybrid vs 18% in CA); median AF duration (22 months in hybrid vs 33 months in CA); CHA2DS2-VASc score >3 (53% in hybrid vs 27% in CA); and congestive heart failure (5% in hybrid vs 27% in CA). Race/ethnicity of participants was not reported. Median procedure time (4 hours 16 minutes vs 2 hours 53 minutes; p<.001) and length of hospital stay (4 days vs 2 days; p<.001) were significantly longer in the hybrid group. Radiation dose (31 $cGycm^2$ vs 67 $cGycm^2$; p=.004) and radiation exposure time (23 minutes vs 1 hour 54 minutes; p<.001) were significantly higher in the CA group. Tables 11 and 12 present a summary of the key characteristics and main results of the HARTCAP-AF trial. Study relevance, design, and conduct limitations are presented in Tables 13 and 14.

Doll et al (2023) reported results of the Combined Endoscopic Epicardial and Percutaneous Endocardial Ablation versus Repeated Catheter Ablation in Patients with PErsistent and Longstanding Persistent Atrial Fibrillation (CEASE-AF, NCT02695277) RCT.[59,] CEASE-AF is a multicenter RCT comparing hybrid combined epicardial and endocardial ablation to standard endocardial CA in 9 hospitals in Germany, Netherlands, United Kingdom, Czech Republic, and Poland between 2015 and 2020 including 154 participants (102 hybrid ablation; 52 standard ablation) with symptomatic, drug refractory persistent AF and left atrial diameter > 4.0 cm or longstanding persistent AF. Participants and study physicians were not blinded to treatment assignment; the core rhythm monitoring laboratory was blinded. In the hybrid CA group, pulmonary veins and left posterior atrial wall were isolated with thoracoscopic epicardial ablation including left atrial appendage exclusion and endocardial touch-up ablation was performed 91 to 180 days afterwards. In the standard CA group, endocardial PV isolation and optional substrate ablation were performed. The primary outcome was freedom from AF, atrial flutter, or atrial tachycardia lasting >30 seconds through 12 months without class I/III anti-arrhythmic drugs except those not exceeding previously failed doses. Rhythm status was assessed with 48-hour Holter monitoring during scheduled visits and symptom-driven monitoring during unscheduled visits. 81% of participants had persistent AF. 75% were male and the mean age was 61 (SD=8) years. Race/ethnicity was not reported. Total procedure duration was significantly longer in the hybrid group (336 minutes, SD=97) compared to the CA group (252 minutes, SD=114, p < 0.001). Through 12-months follow-up, 72% (68/95) in the hybrid group were free from AF versus 39% (20/51) in the CA group (absolute risk difference = 32% (95% CI, 14 to 48; p < 0.001). In persistent AF subgroup, freedom from AF was 73% (56/77) in the hybrid group versus 42% (18/43) in the CA group (absolute risk difference=31% (95% CI, 10 to 48). In the longstanding persistent AF subgroup, freedom from AF was 67% (12/18) in the hybrid group compared to 25% (2/8) in the CA group (absolute risk difference=42% (95% CI, 4 to 73). Composite major complication rates within 30 days after the index procedure and 30 days after the second stage hybrid ablation or repeat standard ablation were 8% (8/102) and 6% (3/52) in the hybrid versus

CA groups (p = 0.751). Through 12-months post-index procedure, composite major complications occurred in 9% (9/102) in the hybrid group versus 6% (3/52) in the CA group (p = 0.752). There was one death (myocardial infarction) in the hybrid group at 93 days post-index procedure. By the 12-month follow-up visit, 4% (4/95) in the hybrid group and 35% (18/51) in the CA group had additional ablation (p < 0.001). Cardioversions (pharmaceutical and electrical) were performed in 12% (11/95) in the hybrid group and 26% (13/51) in the CA group during this time frame (p = 0.037).

Table 11. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	**Comparator**
Jan (2018)[60,]	Slovenia	1	2018	Adults with paroxysmal AF Mean age, 59 years; 26% women	Hybrid Convergent; n=24	CA; n=26
DeLurgio (2020); CONVERGE[56,]	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 and no prior CA Mean age, 64 years; Mean years since diagnosis of AF, 4.4; 70% men; Hispanic or Latino, 2%; 4% Black; 95% White	Hybrid Convergent, n=102	CA, n=51
Lee (2022); EPIREAF[57,]	Korea	1	Jun 2016-Nov2019	Adults with symptomatic, persistent AF refractory or intolerant to antiarrhythmic drugs after prior	Hybrid Convergent, n=50	CA; n=50

Study	Countries	Sites	Dates	Participants	Interventions	
				endocardial ablation Median age, 59 years; 16% women		
van der Heijden (2023); HARTCAP-AF[58,]	Netherlands	1	Oct 2016-Dec 2018	Adults with symptomatic, persistent AF refractory to 1 or more class I or III antiarrhythmic drugs and no prior CA Median age, 64 years	Hybrid; n=19	CA; n=22
Doll (2023); CEASE-AF[59,]	Germany, Netherlands, UK, Czech Republic, Poland	12	November 2015 to May 2020	Adults ≤75 years of age with symptomatic, drug refractory persistent AF and left atrial diameter > 4.0 cm or longstanding persistent AF 75% men; mean age, 61 years	Hybrid; n=102	CA; n=52

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

Table 12. Summary of Key RCT Results

Study	Freedom from AF	AF burden reduction	Cardioversions	Major adverse events
Jan (2018)[60,]	Recurrence of episode of AF/AFL/AT lasting 6 minutes or more Mean follow-up, 30.5 months			Periprocedural complication rates
Hybrid convergent	17% (4/24)	NR	4% (1/24)	12.5%
CA	38% (10/26)	NR	8% (2/26)	0%

Study	Freedom from AF	AF burden reduction	Cardioversions	Major adverse events
Treatment effect	OR=3.78 (1.17 to 12.19); p=.05			
DeLurgio (2020); CONVERGE[56,]	Freedom from AF/atrial flutter/atrial tachycardia absent of class I/II antiarrhythmic drugs 1-year	90% AF burden reduction 1-year	Freedom from cardioversions 1 year	Between 8- and 30-days postprocedure
Hybrid Convergent	67.7% (67/99)	80% (60/75)	91%	7.8% (8/102)
CA	50% (25/50)	56.8% (25/44)	74%	0%
Treatment effect	RD=17.7% (RR, 1.35; p=.036)	RD=23.2% (RR, 1.41; p=.007)	p=.006	p=.0525
DeLurgio (2022); CONVERGE subanalysis[61,]	Long-standing persistent atrial fibrillation subgroup (n=65)			
Hybrid convergent	65.8% (25/38)	78.9% (30/38)		7.9% (3/38)
CA	37.0% (10/27)	46.2% (12/26)		0%
Treatment effect	RD=28.8% (95% CI, 5.1 to 52.4; p=.022)	RD=32.8% (95% CI, 9.7 to 55.9; p=.007)		
Lee (2022); EPIREAF[57,]	Recurrence of sustained (>30 seconds) AF or atrial tachycardia 1 year			Periprocedural complication rate 24 hours
Hybrid convergent	32% (16/50)	NR	NR	2%
CA	42% (21/50)	NR	NR	16%
Treatment effect	HR=0.72 (95% CI, 0.38 to 1.39); p=.33			OR=0.11 (0.00 to 0.87; p=.03
van der Heijden (2023); HARTCAP-AF[58,]	Freedom from any atrial tachyarrhythmia >5 minutes off antiarrhythmic drugs 1 year		Number of cardioversions 1 year	1 year
Hybrid	89% (17/19)	NR	5% (1/19)	1 (pericarditis)
CA	41% (9/22)	NR	23% (5/22)	1 (bleeding)
Treatment effect	p=.002		p=.19	p=1.000

Study	Freedom from AF	AF burden reduction	Cardioversions	Major adverse events
Doll (2023); CEASE-AF[59,]	Freedom from AF, atrial flutter, atrial tachycardia episodes >30 s through 12-months without Class I or III antiarrhythmic drugs	NR	Number of cardioversions by 1 year	Major complications by 1 year
Hybrid	72% (68/95)		12% (11/95)	9% (9/102)
CA	39% (20/51)		26% (13/51)	6% (3/52)
Treatment effect	Risk difference=32% (95% CI, 14 to 48); p<.01		p=.04	p=.75

AF: atrial fibrillation; AFL: atrial flutter;AT: atrial tachycardia; CA: catheter ablation; CI: confidence interval; HR: hazard ratio; RCT: randomized controlled trial; RD: risk difference;OR: odds ratio; RR: risk ratio.

Table 13. Study Relevance Limitations of Key RCTs

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Jan (2018)[60,]	5. Race/ethnicity not reported in publication; study conducted entirely in Slovenia	5. Procedures conducted at a single, highly specialized center			2. Safety only reported short term
DeLurgio (2020); CONVERGE[56,]	5. Study population is 95% White		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	
Lee (2022); EPIREAF[57,]	5. Race/ethnicity not reported in publication; study conducted entirely in Korea	5. Procedures conducted at a single, highly specialized center	4. 7/50 of the CA participants did not undergo the procedure (compared to 0/50 in the hybrid group)	4. Intermittent rhythm monitoring post-procedure	2. Safety only reported at 24 hours

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
van der Heijden (2023); HARTCAP-AF[58,]	5. Race/ethnicity not reported in publication; study conducted entirely in Netherlands	5. Procedures conducted at a single, highly specialized center		4. Intermittent rhythm monitoring post-procedure	
Doll (2023); CEASE-AF[59,]	5. Race/ethnicity not reported in publication	4: In hybrid arm, endocardial procedure was performed 91 to 180 days after epicardial procedure which is a longer interval than typical in the US 5. Expertise of surgeon and electrophysiologist not reported		4. Intermittent rhythm monitoring post-procedure	

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; 5. Enrolled study populations do not reflect relevant diversity; 6. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest; 5. Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[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; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 14. Study Design and Conduct Limitations of Key RCTs

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Jan (2018)[60,]		1. Subjects and clinicians not blinded to treatment assignment				5. High uncertainty about rates of adverse events due to very small number of events and sample size

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
DeLurgio (2020); CONVERGE[56,]	3. Allocation concealment was not described in the publication or the protocol.	1. Subjects and clinicians not blinded to treatment assignment				
Lee (2022); EPIREAF[57,]	3. Allocation concealment was not described	1. Subjects and clinicians not blinded to treatment assignment		1. 13/50 in the hybrid group and 9/50 in the CA group were lost to follow-up before the 1-year primary assessment		4. Data on subsequent procedures (e.g., cardioversion) not provided by treatment group
van der Heijden (2023); HARTCAP-AF[58,]	3. Allocation concealment was not described	1. Subjects and clinicians not blinded to treatment assignment				5. High uncertainty about rates of adverse events due to very small number of events and sample size
Doll (2023); CEASE-AF[59,]		1. Subjects and clinicians not blinded to treatment assignment		1. 19/114 (17%) in hybrid group and 5/56 (9%) were not included in the primary analysis 2,6: Primary analysis in 'modified' ITT population; however, worst case sensitivity analysis was provided		

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; 5. Other.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[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); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[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; 5. Other.

Nonrandomized Studies

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).[62,] 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.[63,] 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.

Pannone et al (2023) reported long-term (~5 year) results of a retrospective analysis of 120 consecutive patients who had one-step hybrid AF ablation in Brussels from 2010 to 2020.[64,] 85 patients underwent hybrid AF ablation as a first procedure (20%, persistent AF, 80% long-standing persistent AF), 20 patients as a second procedure (70%, paroxysmal AF), and 15 patients as a third procedure (67%, paroxysmal AF). At the mean follow-up of 62 months (SD=20), 53% of patients had experienced atrial tachyarrhythmia recurrence. Atrial tachyarrhythmia-free survival without antiarrhythmic drugs was as follows: 77% at 12 months, 68% at 24 months, 61% at 36 months, 54% at 48 months, and 46% at 60 months. Complications occurred in 13% of patients.

Other relevant single-arm case series have included populations ranging from 19 to 104 patients.[65,66,51,67,68,69,70,71,72,73,74,75,76,77,] These series have consistently reported high success rates in maintaining sinus rhythm at 1-year follow-up, ranging from 65% 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 5 RCTs (sample sizes ranging from 41 to 154) and nonrandomized comparative studies that compare a hybrid procedure to a standard percutaneous procedure, a number of single-arm case series, and systematic reviews of these studies. The RCTs varied with respect to the procedure used in the hybrid arm and the populations included (persistent versus paroxysmal AF). 1 RCT (CONVERGE) was conducted in the US and population demographics are not reflective of general US populations. Most trial participants have been male. Results of the RCTs and nonrandomized comparative studies have generally found an increased rate of AF-free survival and reduced need for cardioversion through 1 year with the use of a hybrid procedure as compared to CA in patients with persistent and long-standing AF. The largest RCT (CEASE-AF) reported composite major complications at 1 year in 9% vs 6% with hybrid vs standard ablation.Most RCTs were conducted at highly specialized centers. Observational studies with mid- and long-term follow-up have estimated freedom from AF following a hybrid procedure at about 2 and 5 years to be approximately 74% and 47%, respectively. Pooled evidence from randomized and nonrandomized studies found an increased risk of periprocedural adverse events with the hybrid procedure relative to standard ablation.

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 (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.

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 2023, the Society of Thoracic Surgeons published guidelines on the surgical treatment of atrial fibrillation (AF).[78,] Recommendations are provided in Table 15.

Table 15. Guidelines on Surgical Treatment of Atrial Fibrillation

Recommendation	COR	LOE
Surgical ablation for AF is recommended for first-time non-emergent concomitant mitral operations to restore sinus rhythm and improve long-term outcomes.	I	A
Surgical ablation for AF is recommended for any first-time non-emergent concomitant non-mitral operation to restore sinus rhythm and improve long-term outcomes.	I	B
Surgical ablation for symptomatic AF in the absence of structural heart disease that is refractory to class I/III antiarrhythmic drugs, catheter-based therapy or both is reasonable as a primary stand-alone procedure to restore sinus rhythm.	IIa	B
Surgical ablation for symptomatic persistent or longstanding persistent AF in the absence of structural heart disease is reasonable as a stand-alone procedure using the Cox-Maze III/IV lesion set as the preferred procedure.	IIa	B

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

American Heart Association et al

In 2023, the American Heart Association, American College of Cardiologists, American College of Clinical Pharmacy, and Heart Rhythm Society issued joint guidelines on the diagnosis and management of patients with AF.[79,] Recommendations on the use of surgical ablation to maintain sinus rhythm are provided in Table 16.

Table 16. Guidelines on the Management of Atrial Fibrillation

Recommendation	COR	LOE
For patients with AF who are undergoing cardiac surgery, concomitant surgical ablation can be beneficial to reduce the risk of recurrent AF.	2a	B
For patients with symptomatic, persistent AF refractory to antiarrhythmic drug therapy, a hybrid epicardial and endocardial ablation might be reasonable to reduce the risk of recurrent atrial arrhythmia.	2b	B

AF: atrial fibrillation; COR: class of recommendation; HF: heart failure; LOE: level of evidence.

Heart Rhythm Society et al

A 2024 expert consensus statement on catheter and surgical ablation of atrial fibrillation was developed by the Heart Rhythm Society, European Heart Rhythm Association, Asia Pacific Heart Rhythm Society, and Latin American Heart Rhythm Society.[80,]Recommendations on concomitant surgical ablation in patients undergoing cardiac surgery for other purposes and who have symptomatic AF are provided in Table 17.

Table 17. Guidelines on Concomitant Surgical Ablation in Patients Undergoing Cardiac Surgery[a]

Recommendation	Category of advice	Type of Evidence
Concomitant surgical AF ablation is beneficial in patients with paroxysmal or persistent AF undergoing left atrial open cardiac surgery regardless of prior antiarrhythmic drug failure or intolerance	Advice to do	META
Concomitant surgical AF ablation is beneficial in patients with paroxysmal or persistent AF intolerant or refractory to previous antiarrhythmic drug therapy, undergoing close (non-left atrial open) cardiac surgery	Advice to do	META
Biatrial Cox maze procedure or a minimum of PVI plus left atrial posterior wall isolation is beneficial in patients undergoing surgical AF ablation concomitant to left atrial open cardiac surgery	Advice to do	RAND
Concomitant surgical AF ablation is reasonable in patients with paroxysmal or persistent AF prior to initiation of Class I or III antiarrhythmic therapy, undergoing close (non-left atrial open) cardiac surgery	May be appropriate to do	META

META: Evidence from >1 high-quality RCT or Metaanalyses of high-quality RCTs; RAND: Evidence from 1 high-quality RCT or Evidence from >1 moderate-quality RCT or Metaanalyses of moderate-quality RCTs

The following recommendations were made on stand-alone and hybrid surgical ablation (Table 18).

Table 18. Guidelines on Stand-Alone and Hybrid Surgical Ablation for Symptomatic Atrial Fibrillation

Recommendation[a]	Category of advice	Type of Evidence
Stand-alone surgical or hybrid ablation is reasonable in symptomatic patients with persistent AF with prior unsuccessful catheter ablation and also in those who are intolerant or refractory to antiarrhythmic drug therapy and prefer a surgical/hybrid approach, after careful consideration of relative safety and efficacy of treatment options.	May be appropriate to do	META
Stand-alone surgical or hybrid ablation may be reasonable in symptomatic patients with paroxysmal AF with prior unsuccessful catheter ablations who prefer a surgical/hybrid approach, after careful consideration of relative safety and efficacy of treatment options	Area of uncertainty	RAND

META: Evidence from >1 high-quality RCT or Metaanalyses of high-quality RCTs; RAND: Evidence from 1 high-quality RCT or Evidence from >1 moderate-quality RCT or Metaanalyses of moderate-quality RCTs

American Association for Thoracic Surgery

In 2017, the American Association for Thoracic Surgery published guidelines on surgical ablation for AF.[81,] Recommendations on concomitant surgical ablation in patients with AF are provided in Table 19.

Table 19. 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 20.

Table 20. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03546374	Irrigated Radio Frequency Ablation to Terminate Non-Paroxysmal Atrial Fibrillation (Terminate AF Study)	160	Aug 2024
NCT06165510	Convergent Ablation Plus Left Atrial Appendage Isolation for the Treatment of Persistent Atrial Fibrillation (CLIP-AF)	48	Oct 2025

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT03737929	Comparison of the Efficacy of Hybrid Ablative Therapy for Patients With Persistent Atrial Fibrillation Versus Conventional Catheter Ablation (HT2AF)	228	Dec 2025
NCT05393180	Hybrid Convergent of Epicardial and Endocardial RF Ablation for the Treatment of Symptomatic Longstanding Persistent AF: CONVERGE Post-Approval Study (PAS)	325	Dec 2025
NCT05723536	LAI-AF Trial: Hybrid Endo-epicardial Partial Left Atrial Isolation vs. Endocardial Ablation in Patients With Persistent Atrial Fibrillation (PLAI-AF)	80	Dec 2025
NCT03732794	AtriCure CryoICE Lesions for Persistent and Long-standing Persistent Atrial Fibrillation Treatment During Concomitant On-Pump Endo/Epicardial Cardiac Surgery	150	Dec 2026
NCT05411614	A Randomised Controlled Trial Comparing Hybrid Convergent Ablation to Standard Catheter Ablation in Patients With Non-Paroxysmal Atrial Fibrillation (HALT-AF)	100	Oct 2027
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 2027
NCT04715425	Thoracoscopic Surgical Versus Catheter Ablation Approaches for Primary Treatment of Persistent Atrial Fibrillation	170	Sep 2028
Unpublished			
NCT04237389	Comparative Assessment of Catheter and Thoracoscopic Approaches in Patients With Persistent and Long-standing Persistent Atrial Fibrillation (TACAAF)	60	Aug 2022 (unknown)

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 (e.g., maze procedure); without cardiopulmonary bypass
33256	Operative tissue ablation and reconstruction of atria, extensive (e.g., 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 (e.g., 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 (e.g., 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 (e.g., maze procedure), without cardiopulmonary bypass

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.

REVISIONS	
	Updated Rationale section.
	Updated References section.
08-09-2022	Updated Description Section
	Updated Policy Section ▪ Section B Added: "Stand alone" now reads "Stand-alone minimally invasive, off-pump maze procedures (i.e., modified maze procedures), including those done via mini-thoracotomy, are considered experimental / investigational for the treatment of atrial fibrillation or flutter."
	Update Rationale Section
	Updated References Section
06-27-2023	Updated Description Section
	Update Rationale Section
	Updated Coding Section ▪ Removed ICD-10 Diagnoses Box
	Updated References Section
05-13-2025	Updated Description Section
	Update Rationale Section
	Updated References Section

REFERENCES

1. Miyasaka Y, Barnes ME, Gersh BJ, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. Circulation. Jul 11 2006; 114(2): 119-25. PMID 16818816
2. Colilla S, Crow A, Petkun W, et al. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. Am J Cardiol. Oct 15 2013; 112(8): 1142-7. PMID 23831166
3. Kornej J, Börschel CS, Benjamin EJ, et al. Epidemiology of Atrial Fibrillation in the 21st Century: Novel Methods and New Insights. Circ Res. Jun 19 2020; 127(1): 4-20. PMID 32716709
4. Benjamin EJ, Levy D, Vaziri SM, et al. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. JAMA. Mar 16 1994; 271(11): 840-4. PMID 8114238
5. Heeringa J, van der Kuip DA, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J. Apr 2006; 27(8): 949-53. PMID 16527828
6. Heckbert SR, Austin TR, Jensen PN, et al. Differences by Race/Ethnicity in the Prevalence of Clinically Detected and Monitor-Detected Atrial Fibrillation: MESA. Circ Arrhythm Electrophysiol. Jan 2020; 13(1): e007698. PMID 31934795
7. Calkins H, Hindricks G, Cappato R, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. Europace. Jan 01 2018; 20(1): e1-e160. PMID 29016840
8. Sakurai Y, Kuno T, Yokoyama Y, et al. Late Survival Benefits of Concomitant Surgical Ablation for Atrial Fibrillation During Cardiac Surgery: A Systematic Review and Meta-Analysis. Am J Cardiol. Oct 28 2024; 235: 16-29. PMID 39471966
9. Huffman MD, Karmali KN, Berendsen MA, et al. Concomitant atrial fibrillation surgery for people undergoing cardiac surgery. Cochrane Database Syst Rev. Aug 22 2016; 2016(8): CD011814. PMID 27551927

10. Phan K, Xie A, Tian DH, et al. Systematic review and meta-analysis of surgical ablation for atrial fibrillation during mitral valve surgery. Ann Cardiothorac Surg. Jan 2014; 3(1): 3-14. PMID 24516793
11. Gillinov AM, Gelijns AC, Parides MK, et al. Surgical ablation of atrial fibrillation during mitral-valve surgery. N Engl J Med. Apr 09 2015; 372(15): 1399-409. PMID 25853744
12. Budera P, Straka Z, Osmančík P, et al. Comparison of cardiac surgery with left atrial surgical ablation vs. cardiac surgery without atrial ablation in patients with coronary and/or valvular heart disease plus atrial fibrillation: final results of the PRAGUE-12 randomized multicentre study. Eur Heart J. Nov 2012; 33(21): 2644-52. PMID 22930458
13. Van Breugel HN, Nieman FH, Accord RE, et al. A prospective randomized multicenter comparison on health-related quality of life: the value of add-on arrhythmia surgery in patients with paroxysmal, permanent or persistent atrial fibrillation undergoing valvular and/or coronary bypass surgery. J Cardiovasc Electrophysiol. May 2010; 21(5): 511-20. PMID 19925605
14. Kim KC, Cho KR, Kim YJ, et al. Long-term results of the Cox-Maze III procedure for persistent atrial fibrillation associated with rheumatic mitral valve disease: 10-year experience. Eur J Cardiothorac Surg. Feb 2007; 31(2): 261-6. PMID 17158057
15. Gerdisch M, Lehr E, Dunnington G, et al. Mid-term outcomes of concomitant Cox-Maze IV: Results from a multicenter prospective registry. J Card Surg. Oct 2022; 37(10): 3006-3013. PMID 35870185
16. Damiano RJ, Badhwar V, Acker MA, et al. The CURE-AF trial: a prospective, multicenter trial of irrigated radiofrequency ablation for the treatment of persistent atrial fibrillation during concomitant cardiac surgery. Heart Rhythm. Jan 2014; 11(1): 39-45. PMID 24184028
17. Gaita F, Ebrille E, Scaglione M, et al. Very long-term results of surgical and transcatheter ablation of long-standing persistent atrial fibrillation. Ann Thorac Surg. Oct 2013; 96(4): 1273-1278. PMID 23915587
18. Watkins AC, Young CA, Ghoreishi M, et al. Prospective assessment of the CryoMaze procedure with continuous outpatient telemetry in 136 patients. Ann Thorac Surg. Apr 2014; 97(4): 1191-8; discussion 1198. PMID 24582049
19. McCarthy PM, Gerdisch M, Philpott J, et al. Three-year outcomes of the postapproval study of the AtriCure Bipolar Radiofrequency Ablation of Permanent Atrial Fibrillation Trial. J Thorac Cardiovasc Surg. Aug 2022; 164(2): 519-527.e4. PMID 33129501
20. van Laar C, Kelder J, van Putte BP. The totally thoracoscopic maze procedure for the treatment of atrial fibrillation. Interact Cardiovasc Thorac Surg. Jan 2017; 24(1): 102-111. PMID 27664426
21. Yi S, Liu X, Wang W, et al. Thoracoscopic surgical ablation or catheter ablation for patients with atrial fibrillation? A systematic review and meta-analysis of randomized controlled trials. Interact Cardiovasc Thorac Surg. Dec 07 2020; 31(6): 763-773. PMID 33166993
22. Phan K, Phan S, Thiagalingam A, et al. Thoracoscopic surgical ablation versus catheter ablation for atrial fibrillation. Eur J Cardiothorac Surg. Apr 2016; 49(4): 1044-51. PMID 26003961
23. Boersma LV, Castella M, van Boven W, et al. Atrial fibrillation catheter ablation versus surgical ablation treatment (FAST): a 2-center randomized clinical trial. Circulation. Jan 03 2012; 125(1): 23-30. PMID 22082673

24. Castellá M, Kotecha D, van Laar C, et al. Thoracoscopic vs. catheter ablation for atrial fibrillation: long-term follow-up of the FAST randomized trial. Europace. May 01 2019; 21(5): 746-753. PMID 30715255
25. Pokushalov E, Romanov A, Elesin D, et al. Catheter versus surgical ablation of atrial fibrillation after a failed initial pulmonary vein isolation procedure: a randomized controlled trial. J Cardiovasc Electrophysiol. Dec 2013; 24(12): 1338-43. PMID 24016147
26. Adiyaman A, Buist TJ, Beukema RJ, et al. Randomized Controlled Trial of Surgical Versus Catheter Ablation for Paroxysmal and Early Persistent Atrial Fibrillation. Circ Arrhythm Electrophysiol. Oct 2018; 11(10): e006182. PMID 30354411
27. Haldar S, Khan HR, Boyalla V, et al. Catheter ablation vs. thoracoscopic surgical ablation in long-standing persistent atrial fibrillation: CASA-AF randomized controlled trial. Eur Heart J. Dec 14 2020; 41(47): 4471-4480. PMID 32860414
28. Boyalla V, Haldar S, Khan H, et al. Long-term clinical outcomes and cost-effectiveness of catheter vs thoracoscopic surgical ablation in long-standing persistent atrial fibrillation using continuous cardiac monitoring: CASA-AF randomized controlled trial. Heart Rhythm. Sep 2024; 21(9): 1562-1569. PMID 38763376
29. Kwon HJ, Choi JH, Kim HR, et al. Radiofrequency vs. Cryoballoon vs. Thoracoscopic Surgical Ablation for Atrial Fibrillation: A Single-Center Experience. Medicina (Kaunas). Sep 26 2021; 57(10). PMID 34684060
30. Mahapatra S, LaPar DJ, Kamath S, et al. Initial experience of sequential surgical epicardial-catheter endocardial ablation for persistent and long-standing persistent atrial fibrillation with long-term follow-up. Ann Thorac Surg. Jun 2011; 91(6): 1890-8. PMID 21619988
31. Stulak JM, Dearani JA, Sundt TM, et al. Ablation of atrial fibrillation: comparison of catheter-based techniques and the Cox-Maze III operation. Ann Thorac Surg. Jun 2011; 91(6): 1882-8; discussion 1888-9. PMID 21619987
32. Wang J, Li Y, Shi J, et al. Minimally invasive surgical versus catheter ablation for the long-lasting persistent atrial fibrillation. PLoS One. 2011; 6(7): e22122. PMID 21765943
33. Lawrance CP, Henn MC, Miller JR, et al. A minimally invasive Cox maze IV procedure is as effective as sternotomy while decreasing major morbidity and hospital stay. J Thorac Cardiovasc Surg. Sep 2014; 148(3): 955-61; discussion 962-2. PMID 25048635
34. De Maat GE, Pozzoli A, Scholten MF, et al. Surgical minimally invasive pulmonary vein isolation for lone atrial fibrillation: midterm results of a multicenter study. Innovations (Phila). 2013; 8(6): 410-5. PMID 24356430
35. Massimiano PS, Yanagawa B, Henry L, et al. Minimally invasive fibrillating heart surgery: a safe and effective approach for mitral valve and surgical ablation for atrial fibrillation. Ann Thorac Surg. Aug 2013; 96(2): 520-7. PMID 23773732
36. Cui YQ, Li Y, Gao F, et al. Video-assisted minimally invasive surgery for lone atrial fibrillation: a clinical report of 81 cases. J Thorac Cardiovasc Surg. Feb 2010; 139(2): 326-32. PMID 19660413
37. Edgerton JR, Brinkman WT, Weaver T, et al. Pulmonary vein isolation and autonomic denervation for the management of paroxysmal atrial fibrillation by a minimally invasive surgical approach. J Thorac Cardiovasc Surg. Oct 2010; 140(4): 823-8. PMID 20299028
38. Han FT, Kasirajan V, Kowalski M, et al. Results of a minimally invasive surgical pulmonary vein isolation and ganglionic plexi ablation for atrial fibrillation: single-center experience with 12-month follow-up. Circ Arrhythm Electrophysiol. Aug 2009; 2(4): 370-7. PMID 19808492

39. Pruitt JC, Lazzara RR, Ebra G. Minimally invasive surgical ablation of atrial fibrillation: the thoracoscopic box lesion approach. J Interv Card Electrophysiol. Dec 2007; 20(3): 83-7. PMID 18214660
40. Sirak J, Jones D, Sun B, et al. Toward a definitive, totally thoracoscopic procedure for atrial fibrillation. Ann Thorac Surg. Dec 2008; 86(6): 1960-4. PMID 19022018
41. Speziale G, Bonifazi R, Nasso G, et al. Minimally invasive radiofrequency ablation of lone atrial fibrillation by monolateral right minithoracotomy: operative and early follow-up results. Ann Thorac Surg. Jul 2010; 90(1): 161-7. PMID 20609767
42. Wudel JH, Chaudhuri P, Hiller JJ. Video-assisted epicardial ablation and left atrial appendage exclusion for atrial fibrillation: extended follow-up. Ann Thorac Surg. Jan 2008; 85(1): 34-8. PMID 18154774
43. Yilmaz A, Geuzebroek GS, Van Putte BP, et al. Completely thoracoscopic pulmonary vein isolation with ganglionic plexus ablation and left atrial appendage amputation for treatment of atrial fibrillation. Eur J Cardiothorac Surg. Sep 2010; 38(3): 356-60. PMID 20227287
44. Yilmaz A, Van Putte BP, Van Boven WJ. Completely thoracoscopic bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. J Thorac Cardiovasc Surg. Aug 2008; 136(2): 521-2. PMID 18692667
45. Geuzebroek GS, Bentala M, Molhoek SG, et al. Totally thoracoscopic left atrial Maze: standardized, effective and safe. Interact Cardiovasc Thorac Surg. Mar 2016; 22(3): 259-64. PMID 26705300
46. Vos LM, Bentala M, Geuzebroek GS, et al. Long-term outcome after totally thoracoscopic ablation for atrial fibrillation. J Cardiovasc Electrophysiol. Jan 2020; 31(1): 40-45. PMID 31691391
47. Harlaar N, Oudeman MA, Trines SA, et al. Long-term follow-up of thoracoscopic ablation in long-standing persistent atrial fibrillation. Interact Cardiovasc Thorac Surg. Jun 01 2022; 34(6): 990-998. PMID 34957518
48. Ad N, Henry L, Hunt S, et al. The outcome of the Cox Maze procedure in patients with previous percutaneous catheter ablation to treat atrial fibrillation. Ann Thorac Surg. May 2011; 91(5): 1371-7; discussion 1377. PMID 21457939
49. Castellá M, Pereda D, Mestres CA, et al. Thoracoscopic pulmonary vein isolation in patients with atrial fibrillation and failed percutaneous ablation. J Thorac Cardiovasc Surg. Sep 2010; 140(3): 633-8. PMID 20117799
50. MacGregor RM, Bakir NH, Pedamallu H, et al. Late results after stand-alone surgical ablation for atrial fibrillation. J Thorac Cardiovasc Surg. Nov 2022; 164(5): 1515-1528.e8. PMID 34045056
51. Bisleri G, Rosati F, Bontempi L, et al. Hybrid approach for the treatment of long-standing persistent atrial fibrillation: electrophysiological findings and clinical results. Eur J Cardiothorac Surg. Nov 2013; 44(5): 919-23. PMID 23475587
52. Winkle RA, Mead RH, Engel G, et al. Very long term outcomes of atrial fibrillation ablation. Heart Rhythm. May 2023; 20(5): 680-688. PMID 36764350
53. Eranki A, Wilson-Smith A, Flynn C, et al. Mid term freedom from atrial fibrillation following hybrid ablation, a systematic review and meta analysis. J Cardiothorac Surg. Apr 19 2023; 18(1): 155. PMID 37076929
54. Mhanna M, Beran A, Al-Abdouh A, et al. Hybrid convergent ablation versus endocardial catheter ablation for atrial fibrillation: A systematic review and meta-analysis. J Arrhythm. Dec 2021; 37(6): 1459-1467. PMID 34887950

55. Eranki A, Wilson-Smith AR, Williams ML, et al. Hybrid convergent ablation versus endocardial catheter ablation for atrial fibrillation: a systematic review and meta-analysis of randomised control trials and propensity matched studies. J Cardiothorac Surg. Aug 13 2022; 17(1): 181. PMID 35964093
56. DeLurgio DB, Crossen KJ, Gill J, et al. Hybrid Convergent Procedure for the Treatment of Persistent and Long-Standing Persistent Atrial Fibrillation: Results of CONVERGE Clinical Trial. Circ Arrhythm Electrophysiol. Dec 2020; 13(12): e009288. PMID 33185144
57. Lee KN, Kim DY, Boo KY, et al. Combined epicardial and endocardial approach for redo radiofrequency catheter ablation in patients with persistent atrial fibrillation: a randomized clinical trial. Europace. Oct 13 2022; 24(9): 1412-1419. PMID 35640923
58. van der Heijden CAJ, Weberndörfer V, Vroomen M, et al. Hybrid Ablation Versus Repeated Catheter Ablation in Persistent Atrial Fibrillation: A Randomized Controlled Trial. JACC Clin Electrophysiol. Jul 2023; 9(7 Pt 2): 1013-1023. PMID 36752455
59. Doll N, Weimar T, Kosior DA, et al. Efficacy and safety of hybrid epicardial and endocardial ablation versus endocardial ablation in patients with persistent and longstanding persistent atrial fibrillation: a randomised, controlled trial. EClinicalMedicine. Jul 2023; 61: 102052. PMID 37425372
60. Jan M, Žižek D, Geršak ŽM, et al. Comparison of treatment outcomes between convergent procedure and catheter ablation for paroxysmal atrial fibrillation evaluated with implantable loop recorder monitoring. J Cardiovasc Electrophysiol. Aug 2018; 29(8): 1073-1080. PMID 29722468
61. DeLurgio DB, Blauth C, Halkos ME, et al. Hybrid epicardial-endocardial ablation for long-standing persistent atrial fibrillation: A subanalysis of the CONVERGE Trial. Heart Rhythm O2. Feb 2023; 4(2): 111-118. PMID 36873309
62. Kress DC, Erickson L, Choudhuri I, et al. Comparative Effectiveness of Hybrid Ablation Versus Endocardial Catheter Ablation Alone in Patients With Persistent Atrial Fibrillation. JACC Clin Electrophysiol. Apr 2017; 3(4): 341-349. PMID 29759446
63. Maclean E, Yap J, Saberwal B, et al. The convergent procedure versus catheter ablation alone in longstanding persistent atrial fibrillation: A single centre, propensity-matched cohort study. Int J Cardiol. Mar 15 2020; 303: 49-53. PMID 32063280
64. Pannone L, Mouram S, Della Rocca DG, et al. Hybrid atrial fibrillation ablation: long-term outcomes from a single-centre 10-year experience. Europace. May 19 2023; 25(5). PMID 37246904
65. Mannakkara NN, Porter B, Child N, et al. Convergent ablation for persistent atrial fibrillation: outcomes from a single-centre real-world experience. Eur J Cardiothorac Surg. Dec 02 2022; 63(1). PMID 36346176
66. Kiankhooy A, Pierce C, Burk S, et al. Hybrid ablation of persistent and long-standing persistent atrial fibrillation with depressed ejection fraction: A single-center observational study. JTCVS Open. Dec 2022; 12: 137-146. PMID 36590727
67. Gehi AK, Mounsey JP, Pursell I, et al. Hybrid epicardial-endocardial ablation using a pericardioscopic technique for the treatment of atrial fibrillation. Heart Rhythm. Jan 2013; 10(1): 22-8. PMID 23064043
68. Gersak B, Pernat A, Robic B, et al. Low rate of atrial fibrillation recurrence verified by implantable loop recorder monitoring following a convergent epicardial and endocardial ablation of atrial fibrillation. J Cardiovasc Electrophysiol. Oct 2012; 23(10): 1059-66. PMID 22587585

69. La Meir M, Gelsomino S, Lorusso R, et al. The hybrid approach for the surgical treatment of lone atrial fibrillation: one-year results employing a monopolar radiofrequency source. J Cardiothorac Surg. Jul 19 2012; 7: 71. PMID 22812613
70. Muneretto C, Bisleri G, Bontempi L, et al. Successful treatment of lone persistent atrial fibrillation by means of a hybrid thoracoscopic-transcatheter approach. Innovations (Phila). 2012; 7(4): 254-8. PMID 23123991
71. Muneretto C, Bisleri G, Bontempi L, et al. Durable staged hybrid ablation with thoracoscopic and percutaneous approach for treatment of long-standing atrial fibrillation: a 30-month assessment with continuous monitoring. J Thorac Cardiovasc Surg. Dec 2012; 144(6): 1460-5; discussion 1465. PMID 23062968
72. Pison L, La Meir M, van Opstal J, et al. Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. J Am Coll Cardiol. Jul 03 2012; 60(1): 54-61. PMID 22742400
73. Zembala M, Filipiak K, Kowalski O, et al. Minimally invasive hybrid ablation procedure for the treatment of persistent atrial fibrillation: one year results. Kardiol Pol. 2012; 70(8): 819-28. PMID 22933215
74. Geršak B, Zembala MO, Müller D, et al. European experience of the convergent atrial fibrillation procedure: multicenter outcomes in consecutive patients. J Thorac Cardiovasc Surg. Apr 2014; 147(4): 1411-6. PMID 23988287
75. Civello KC, Smith CA, Boedefeld W. Combined endocardial and epicardial ablation for symptomatic atrial fibrillation: single center experience in 100+ consecutive patients. J Innovations Cardiac Rhythm Manage. 2013;August.
76. Tonks R, Lantz G, Mahlow J, et al. Short and Intermediate Term Outcomes of the Convergent Procedure: Initial Experience in a Tertiary Referral Center. Ann Thorac Cardiovasc Surg. Feb 20 2020; 26(1): 13-21. PMID 31495813
77. Carpenter A, Pannell LMK, Rizvi SIA, et al. Convergent approach to persistent atrial fibrillation ablation: long-term single-centre safety and efficacy. Front Cardiovasc Med. 2023; 10: 1336801. PMID 38390303
78. Wyler von Ballmoos MC, Hui DS, Mehaffey JH, et al. The Society of Thoracic Surgeons 2023 Clinical Practice Guidelines for the Surgical Treatment of Atrial Fibrillation. Ann Thorac Surg. Jan 27 2024. PMID 38286206
79. Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. Jan 02 2024; 149(1): e1-e156. PMID 38033089
80. Tzeis S, Gerstenfeld EP, Kalman J, et al. 2024 European Heart Rhythm Association/Heart Rhythm Society/Asia Pacific Heart Rhythm Society/Latin American Heart Rhythm Society expert consensus statement on catheter and surgical ablation of atrial fibrillation. Europace. Mar 30 2024; 26(4). PMID 38587017
81. Ad N, Damiano RJ, Badhwar V, et al. Expert consensus guidelines: Examining surgical ablation for atrial fibrillation. J Thorac Cardiovasc Surg. Jun 2017; 153(6): 1330-1354.e1. PMID 28390766

OTHER REFERENCES

1. Blue Cross and Blue Shield of Kansas Cardiology Liaison Committee, July 2019; January 2020, May 2021, July 2022.