MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

Medical Policy

Catheter Ablation as Treatment for Atrial Fibrillation

Table of Contents

Policy Number: 141

BCBSA Reference Number: 2.02.19
NCD/LCD: N/A

Related Policies

- Catheter Ablation of other Arrhythmogenic Foci #123
- Open and Thoracoscopic Approaches to Treat Atrial Fibrillation - Maze and Related Procedures, #356
- Left-Atrial Appendage Closure Devices for Stroke Prevention in Atrial Fibrillation, #334

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue[SM] and Medicare PPO Blue[SM] Members

Transcatheter radiofrequency ablation or cryoablation to treat atrial fibrillation may be **MEDICALLY NECESSARY** as a treatment for either of the following indications which have failed to respond to adequate trials of antiarrhythmic medications:

- Symptomatic paroxysmal or symptomatic persistent atrial fibrillation, **or**
- As an alternative to atrioventricular nodal ablation and pacemaker insertion in patients with class II or III congestive heart failure and symptomatic atrial fibrillation.

Transcatheter radiofrequency ablation or cryoablation to treat atrial fibrillation may be considered **MEDICALLY NECESSARY** as an initial treatment for patients with recurrent symptomatic paroxysmal atrial fibrillation (>1 episode, with 4 or fewer episodes in the previous 6 months) in whom a rhythm-control strategy is desired.

Up to 3 repeat radiofrequency ablations or cryoablations may be considered **MEDICALLY NECESSARY** in patients with recurrence of atrial fibrillation and/or development of atrial flutter following the initial procedure.

Transcatheter radiofrequency ablation or cryoablation to treat atrial fibrillation is considered **INVESTIGATIONAL** as a treatment for cases of atrial fibrillation that do not meet the criteria outlined above.

Transcatheter treatment of atrial fibrillation may include pulmonary vein isolation and/or focal ablation.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO and Indemnity	Prior authorization is **not required**.
Medicare HMO Blue℠	Prior authorization is **not required**.
Medicare PPO Blue℠	Prior authorization is **not required**.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code 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 as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
93656	Comprehensive electrophysiologic evaluation including transseptal catheterizations, insertion and repositioning of multiple electrode catheters with induction or attempted induction of an arrhythmia including left or right atrial pacing,/recording when necessary, right ventricular pacing/recording when necessary, and His bundle recording when necessary with intracardiac catheter ablation of atrial fibrillation by pulmonary vein isolation
93657	Additional linear or focal intracardiac catheter ablation of the left or right atrium for treatment of atrial fibrillation remaining after completion of pulmonary vein isolation (List separately in addition to code for primary procedure)

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT codes above if medical necessity criteria are met:

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
I48.0	Paroxysmal atrial fibrillation
I48.1	Persistent atrial fibrillation
I48.2	Chronic atrial fibrillation
I48.3	Typical atrial flutter

I48.4	Atypical atrial flutter
I48.91	Unspecified atrial fibrillation
I48.92	Unspecified atrial flutter
I50.20	Unspecified systolic (congestive) heart failure
I50.21	Acute systolic (congestive) heart failure
I50.22	Chronic systolic (congestive) heart failure
I50.23	Acute or chronic systolic (congestive) heart failure
I50.30	Unspecified diastolic (congestive) heart failure
I50.31	Acute diastolic (congestive) heart failure
I50.32	Chronic diastolic (congestive) heart failure
I50.33	Acute on chronic diastolic (congestive) heart failure
I50.40	Unspecified combined systolic (congestive) and diastolic (congestive) heart failure
I50.41	Acute combined systolic (congestive) and diastolic (congestive) heart failure
I50.42	Chronic combined systolic (congestive) and diastolic (congestive) heart failure
I50.43	Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure
I50.9	Heart failure, unspecified

Description

ATRIAL FIBRILLATION

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with an estimated prevalence of 0.4% of the population, increasing with age. The underlying mechanism of AF involves the interplay between electrical triggering events and the myocardial substrate that permits propagation and maintenance of the aberrant electrical circuit. The most common focal trigger of AF appears to be located within the cardiac muscle that extends into the pulmonary veins.

AF accounts for approximately one-third of hospitalizations for cardiac rhythm disturbances. Symptoms of AF (eg, palpitations, decreased exercise tolerance, dyspnea) are primarily related to poorly controlled or irregular heart rate. The loss of atrioventricular (AV) synchrony results in a decreased cardiac output, which can be significant in patients with compromised cardiac function. Also, patients with AF are at higher risk for stroke, with anticoagulation is typically recommended. AF is also associated with other cardiac conditions, such as valvular heart disease, heart failure, hypertension, and diabetes. Although episodes of AF can be converted to normal sinus rhythm using pharmacologic or electroshock conversion, the natural history of AF is that of recurrence, thought to be related to fibrillation-induced anatomic and electrical remodeling of the atria.

AF can be subdivided into 3 types:

- paroxysmal (episodes that last <7 days and are self-terminating),
- persistent (episodes that last for >7 days and can be terminated pharmacologically or by electrical cardioversion), or
- permanent.

Treatment Strategies

Treatment strategies can be broadly subdivided into rate control, in which only the ventricular rate is controlled, and the atria are allowed to fibrillate, or rhythm control, in which there is an attempt to reestablish and maintain normal sinus rhythm. Rhythm control has long been considered an important treatment goal for management of AF, although its primacy has recently been challenged by the results of several randomized trials reporting that pharmacologically maintained rhythm control offered no improvement in mortality or cardiovascular morbidity compared with rate control.

Currently, the main indications for a rhythm-control strategy are for patients with paroxysmal or persistent AF who have hemodynamic compromise associated with episodes of AF or who have bothersome symptoms, despite adequate rate control. A rhythm-control strategy involves initial pharmacologic or electronic cardioversion, followed by pharmacologic treatment to maintain normal sinus rhythm. However, antiarrhythmic medications are often not effective in maintaining sinus rhythm. As a result, episodes of recurrent AF are typical, and patients with persistent AF may require multiple

episodes of cardioversion. Implantable atrial defibrillators, which are designed to detect and terminate an episode of AF, are an alternative in patients otherwise requiring serial cardioversions, but they have not yet achieved widespread use. Patients with paroxysmal AF, by definition, do not require cardioversion but may be treated pharmacologically to prevent further arrhythmic episodes.

Treatment of permanent AF focuses on rate control, using either pharmacologic therapy or ablation of the AV node, followed by ventricular pacing. Although AV nodal ablation produces symptomatic improvement, it entails lifelong anticoagulation (due to ongoing fibrillation of the atria), loss of AV synchrony, and lifelong pacemaker dependency. Implantable defibrillators are contraindicated in patients with permanent AF.

The treatment options above are not curative. A variety of ablative procedures have been investigated as potentially curative approaches, or modifying the arrhythmia so that drug therapy becomes more effective. Ablative approaches focus on interruption of the electrical pathways that contribute to AF through modifying the arrhythmia triggers and/or the myocardial substrate that maintains the aberrant rhythm. The maze procedure, an open surgical procedure often combined with other cardiac surgeries (eg, valve repair), is an ablative treatment that involves sequential atriotomy incisions designed to create electrical barriers that prevent the maintenance of AF. Because of the highly invasive nature of this procedure, it is currently mainly reserved for patients undergoing open heart surgery for other reasons (eg, valve repair, coronary artery bypass grafting).

Catheter Ablation for AF

Radiofrequency ablation (RFA) using a percutaneous catheter-based approach is widely used to treat a variety of supraventricular arrhythmias, in which intracardiac mapping identifies a discrete arrhythmogenic focus that is the target of ablation (see MP 123). The situation is more complex for AF because there is no single arrhythmogenic focus. Since the inception of ablation techniques in the early 1990s, there has been a progressive understanding of the underlying electrical pathways in the heart associated with AF. In the late 1990s, it was recognized that AF most frequently arises from an abnormal focus at or near the junction of the pulmonary veins and the left atrium, thus leading to the feasibility of more focused, percutaneous ablation techniques. Strategies that have emerged for focal ablation within the pulmonary veins originally involved segmental ostial ablation guided by pulmonary vein potential (electrical approach) but currently more typically involve circumferential pulmonary vein ablation (anatomic approach).

The individual lesion set (in addition to the pulmonary vein isolation) and the degree to which the pulmonary vein antrum is electrically isolated vary. Research into specific ablation and pulmonary vein isolation techniques is ongoing. Evidence from a randomized controlled trial comparing pulmonary vein isolation alone with pulmonary vein isolation plus ablation to treat patients who had electrograms showing complex fractionated activity, and to pulmonary vein isolation plus additional linear ablation across the left atrial roof and mitral valve isthmus, has suggested that the more extensive lesion sets do not reduce the AF recurrence rate.[1] Meta-analyses have found that the addition of complex fractionated atrial electrogram ablation to pulmonary vein isolation alone has not improved rates of freedom from recurrent AF, although the randomized controlled trial by Theis et al (2015) reported that patients with ablation of dormant conduction sources outside the pulmonary veins had fewer arrhythmia recurrences than those treated with pulmonary vein isolation alone.

Circumferential pulmonary vein ablation using radiofrequency energy is the most common approach at present. The procedure also can be done using cryoablation technology. Use of current radiofrequency catheters for AF has a steep learning curve because they require extensive guiding to multiple ablation points. One of the potential advantages of cryoablation is that cryoablation catheters have a circular or shaped end point, permitting a “one-shot” ablation. Other types of radiofrequency catheters, which incorporate circular or otherwise shaped end points, may also be used.

Repeat Procedures

Repeat procedures following initial RFA are commonly performed if AF recurs or if atrial flutter develops postprocedure. The need for repeat procedures may, in part, depend on the clinical characteristics of the patient (eg, age, persistent vs paroxysmal AF, atrial dilatation), and the type of ablation initially performed. Repeat procedures are generally more limited in scope than the initial procedure. For

example, in cases where electrical reconnections occur as a result of incomplete ablation lines, a ”touch up” procedure is done to correct gaps in the original ablation. In other cases when atrial flutter has developed after ablation, a "flutter ablation” is performed, which is more limited than the original AF procedure. A number of clinical and demographic factors are associated with the need for a second procedure, including age, length of AF, permanent AF, left atrial size, and left ventricular ejection fraction.

Outcome Assessment in AF

Various outcomes for the treatment of AF may be considered. The mortality and morbidity related to AF (eg, cardiovascular mortality, stroke, heart failure) are the most important clinical outcomes. However, they are uncommon events, and currently available trials have not been powered to detect differences in these outcomes. Quality of life (QOL) is also an important outcome because QOL measures reflect important manifestations of AF, such as symptoms and reduced exercise tolerance. AF has been shown to be associated with lower QOL scores, and maintenance of sinus rhythm has been associated with higher QOL scores for patients with paroxysmal AF.

Recurrence of AF is a more problematic outcome measure because the intermittent and often transient nature of recurrences makes accurate measurement difficult. This outcome measure has been reported in different ways. For example, the proportion of patients in sinus rhythm at the end of the study, the time to the first recurrence, and the number of recurrences within a period have been reported. Shemin et al (2007) highlighted the difficulties in measuring AF recurrence and recommended a measure of AF “burden,” defined as the percentage of time an individual is in AF, as the optimal measure of treatment efficacy. However, this parameter requires continuous monitoring over a relatively long period, which is inconvenient for patients, resource intensive, and usually not pragmatic in patients who do not already have an implanted pacemaker.

Recommendations for outcome assessment in trials of AF treatment were included in the 2006 American College of Cardiology, American Heart Association, and European Society of Cardiology practice guidelines for the treatment of AF. These guidelines pointed out that the appropriate end points for evaluation of treatment efficacy in patients with paroxysmal or persistent AF have little in common. For example, in studies of persistent AF, the proportion of patients in sinus rhythm at the end of follow-up is a useful end point, but this end point is less useful in studies of paroxysmal AF. Given all these variables, ideally, controlled clinical trials would report a range of outcomes (including QOL) and complications in homogeneous patient groups and compare them with the most relevant treatment alternatives (eg, pharmacologic therapy, defibrillator therapy, AV nodal ablation), depending on the classification of AF (paroxysmal, persistent, permanent).

Summary

For individuals who have symptomatic paroxysmal or persistent AF who have failed antiarrhythmic drugs who receive RFA or cryoablation, the evidence includes multiple randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are overall survival, symptoms, morbid events, and quality of life. RCTs that compare RFA with antiarrhythmic medications have reported that freedom from AF is more likely after ablation than after medications. Results of long-term follow-up (5-6 years) after ablation has demonstrated that late recurrences continue to occur in patients who are free of AF at 1 year. However, most patients who are AF-free at 1 year remain AF-free at 5 to 6 years. Multiple RCTs comparing cryoablation and RFA have found that cryoablation is noninferior to RFA for AF control. RFA and cryoablation differ in adverse effect profiles; for example, cryoablation is associated with higher rates of phrenic nerve paralysis, but may allow a shorter procedure time. Given currently available data, it would be reasonable to consider both RFA and cryoablation effective for catheter ablation of AF foci or pulmonary vein isolation, provided that there is a discussion about the risks and benefits of each. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have symptomatic AF and congestive heart failure who have failed rate control and antiarrhythmic drugs who receive RFA or cryoablation, the evidence includes a TEC Assessment, supported by RCTs. Relevant outcomes are overall survival, symptoms, morbid events, and quality of life. Based on 1 available multicenter RCT, the TEC Assessment found that the evidence was sufficient to

conclude that catheter ablation improves outcomes more than the alternative, atrioventricular (AV) nodal ablation and pacemaker insertion. Findings from this RCT have been supported by other comparative studies, which have reported improvements in AF. It is reasonable to consider both RFA and cryoablation effective for catheter ablation of AF foci or pulmonary vein isolation, provided that there is a discussion about the risks and benefits of each. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have recurrent symptomatic paroxysmal AF who receive RFA or cryoablation as an initial rhythm-control strategy, the evidence includes RCTs and systematic reviews. Relevant outcomes are overall survival, symptoms, morbid events, and quality of life. Two RCTs with low risk of bias compared catheter ablation for pulmonary vein isolation to antiarrhythmic medications. One RCT demonstrated reduced rates of AF recurrence, while the other reported reduced cumulative overall AF burden. Together, these results suggest that, when a rhythm-control strategy is desired, catheter ablation is a reasonable alternative to antiarrhythmic drug therapy. While the RCTs comparing ablation to medical therapy were conducted using RFA, it is reasonable to consider both RFA and cryoablation effective for catheter ablation of AF foci or pulmonary vein isolation, provided that there is a discussion about the risks and benefits of each. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

Policy History

Date	Action
6/2018	New references added from BCBSA National medical policy. Background and summary clarified.
2/2018	Clarified coding information.
6/2017	New references added from BCBSA National medical policy.
8/2016	BCBSA National medical policy review. Last paragraph in Background section revised to remove redundant language and add clarity. 8/2016
7/2016	BCBSA National medical policy review. Policy statement for ablation as first-line therapy for paroxysmal atrial fibrillation clarified to state that the atrial fibrillation should be recurrent. 7/1/2016
11/2015	BCBSA National medical policy review. New medically necessary indications described. Effective 11/1/2015.
5/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
5/2014	New references from BCBSA National medical policy; policy title changed.
5/2013	New references from BCBSA National medical policy.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
4/2011	Reviewed - Medical Policy Group – Cardiology and Pulmonology. No changes to policy statements.
4/2010	Reviewed - Medical Policy Group - Cardiology. No changes to policy statements.
12/2009	BCBS Association National Policy Review. Clarified repeat procedures; non-coverage language was clarified.
11/1/2009	Medical Policy 141 effective 11/1/2009. This treatment was previously addressed on medical policy #123, Catheter Ablation of Other Arrhythmogenic Foci.
11/1/2009	Updated to add coverage of radiofrequency ablation of the pulmonary vein for treatment of atrial fibrillation for commercial products, Medicare HMO Blue, and Medicare PPO Blue effective 11/1/2009.
4/2009	Reviewed - Medical Policy Group – Cardiology. No changes to policy statements.
4/2009	BCBS Association National Policy Review.

	BCBSA now covers for specific indications; BCBSMA will benchmark the BCBSA medical policy effective 11/1/2009 as published in the August 2009 Provider Focus.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

1. Verma A, Jiang CY, Betts TR, et al. Approaches to catheter ablation for persistent atrial fibrillation. *N Engl J Med.* May 7 2015;372(19):1812-1822. PMID 25946280
2. Fadahunsi O, Talabi T, Olowoyeye A, et al. Ablation of complex fractionated atrial electrograms for atrial fibrillation rhythm control: a systematic review and meta-analysis. *Can J Cardiol.* Jun 2016;32(6):791-802. PMID 26514747
3. Providencia R, Lambiase PD, Srinivasan N, et al. Is there still a role for complex fractionated atrial electrogram ablation in addition to pulmonary vein isolation in patients with paroxysmal and persistent atrial fibrillation? meta-analysis of 1415 patients. *Circ Arrhythm Electrophysiol.* Oct 2015;8(5):1017-1029. PMID 26082515
4. Hu X, Jiang J, Ma Y, et al. Is there still a role for additional linear ablation in addition to pulmonary vein isolation in patients with paroxysmal atrial fibrillation? An updated meta-analysis of randomized controlled trials. *Int J Cardiol.* Apr 15 2016;209:266-274. PMID 26897081
5. Scott PA, Silberbauer J, Murgatroyd FD. The impact of adjunctive complex fractionated atrial electrogram ablation and linear lesions on outcomes in persistent atrial fibrillation: a meta-analysis. *Europace.* Mar 2016;18(3):359-367. PMID 26559915
6. Theis C, Konrad T, Mollnau H, et al. Arrhythmia termination versus elimination of dormant pulmonary vein conduction as a procedural end point of catheter ablation for paroxysmal atrial fibrillation: a prospective randomized trial. *Circ Arrhythm Electrophysiol.* Oct 2015;8(5):1080-1087. PMID 26297786
7. Shemin RJ, Cox JL, Gillinov AM, et al. Guidelines for reporting data and outcomes for the surgical treatment of atrial fibrillation. *Ann Thorac Surg.* Mar 2007;83(3):1225-1230. PMID 17307507
8. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation--executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). *J Am Coll Cardiol.* Aug 15 2006;48(4):854-906. PMID 16904574
9. Lee MA, Weachter R, Pollak S, et al. The effect of atrial pacing therapies on atrial tachyarrhythmia burden and frequency: results of a randomized trial in patients with bradycardia and atrial tachyarrhythmias. *J Am Coll Cardiol.* Jun 4 2003;41(11):1926-1932. PMID 12798559
10. Kay GN, Ellenbogen KA, Giudici M, et al. The Ablate and Pace Trial: a prospective study of catheter ablation of the AV conduction system and permanent pacemaker implantation for treatment of atrial fibrillation. APT Investigators. *J Interv Card Electrophysiol.* Jun 1998;2(2):121-135. PMID 9870004
11. Falk RH. Management of atrial fibrillation--radical reform or modest modification? *N Engl J Med.* Dec 5 2002;347(23):1883-1884. PMID 12466514
12. Van Gelder IC, Hagens VE, Bosker HA, et al. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *N Engl J Med.* Dec 5 2002;347(23):1834-1840. PMID 12466507
13. Wyse DG, Waldo AL, DiMarco JP, et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med.* Dec 5 2002;347(23):1825-1833. PMID 12466506
14. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Catheter ablation of the pulmonary veins as a treatment for atrial fibrillation. *TEC Assessments.* 2008;Volume 23:Tab 11.

15. Jais P, Cauchemez B, Macle L, et al. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. *Circulation.* Dec 9 2008;118(24):2498-2505. PMID 19029470
16. Khan MN, Jais P, Cummings J, et al. Pulmonary-vein isolation for atrial fibrillation in patients with heart failure. *N Engl J Med.* Oct 23 2008;359(17):1778-1785. PMID 18946063
17. Oral H, Pappone C, Chugh A, et al. Circumferential pulmonary-vein ablation for chronic atrial fibrillation. *N Engl J Med.* Mar 2 2006;354(9):934-941. PMID 16510747
18. Pappone C, Augello G, Sala S, et al. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal atrial fibrillation: the APAF Study. *J Am Coll Cardiol.* Dec 5 2006;48(11):2340-2347. PMID 17161267
19. Stabile G, Bertaglia E, Senatore G, et al. Catheter ablation treatment in patients with drug-refractory atrial fibrillation: a prospective, multi-centre, randomized, controlled study (Catheter Ablation For The Cure Of Atrial Fibrillation Study). *Eur Heart J.* Jan 2006;27(2):216-221. PMID 16214831
20. Wazni OM, Marrouche NF, Martin DO, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. *JAMA.* Jun 1 2005;293(21):2634-2640. PMID 15928285
21. Nyong J, Amit G, Adler AJ, et al. Efficacy and safety of ablation for people with non-paroxysmal atrial fibrillation. *Cochrane Database Syst Rev.* Nov 22 2016;11:CD012088. PMID 27871122
22. Forleo GB, Mantica M, De Luca L, et al. Catheter ablation of atrial fibrillation in patients with diabetes mellitus type 2: results from a randomized study comparing pulmonary vein isolation versus antiarrhythmic drug therapy. *J Cardiovasc Electrophysiol.* Jan 2009;20(1):22-28. PMID 18775050
23. Mont L, Bisbal F, Hernandez-Madrid A, et al. Catheter ablation vs. antiarrhythmic drug treatment of persistent atrial fibrillation: a multicentre, randomized, controlled trial (SARA study). *Eur Heart J.* Feb 2014;35(8):501-507. PMID 24135832
24. Vaidya K, Arnott C, Russell A, et al. Pulmonary vein isolation compared to rate control in patients with atrial fibrillation: a systematic review and meta-analysis. *Heart Lung Circ.* Aug 2015;24(8):744-752. PMID 25890871
25. Shi LZ, Heng R, Liu SM, et al. Effect of catheter ablation versus antiarrhythmic drugs on atrial fibrillation: A meta-analysis of randomized controlled trials. *Exp Ther Med.* Aug 2015;10(2):816-822. PMID 26622399
26. Chen HS, Wen JM, Wu SN, et al. Catheter ablation for paroxysmal and persistent atrial fibrillation. *Cochrane Database Syst Rev.* Apr 18 2012;4(4):CD007101. PMID 22513945
27. Ganesan AN, Shipp NJ, Brooks AG, et al. Long-term outcomes of catheter ablation of atrial fibrillation: a systematic review and meta-analysis. *J Am Heart Assoc.* Apr 2013;2(2):e004549. PMID 23537812
28. Noheria A, Kumar A, Wylie JV, Jr., et al. Catheter ablation vs antiarrhythmic drug therapy for atrial fibrillation: a systematic review. *Arch Intern Med.* Mar 24 2008;168(6):581-586. PMID 18362249
29. Gjesdal K, Vist GE, Bugge E, et al. Curative ablation for atrial fibrillation: a systematic review. *Scand Cardiovasc J.* Feb 2008;42(1):3-8. PMID 18273730
30. Nair GM, Nery PB, Diwakaramenon S, et al. A systematic review of randomized trials comparing radiofrequency ablation with antiarrhythmic medications in patients with atrial fibrillation. *J Cardiovasc Electrophysiol.* Feb 2009;20(2):138-144. PMID 18775040
31. Zhuang Y, Yong YH, Chen ML. Updating the evidence for the effect of radiofrequency catheter ablation on left atrial volume and function in patients with atrial fibrillation: a meta-analysis. *JRSM Open.* Mar 2014;5(3):2054270414521185. PMID 25057380
32. Wilber DJ, Pappone C, Neuzil P, et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. *JAMA.* Jan 27 2010;303(4):333-340. PMID 20103757
33. Marrouche NF, Brachmann J, Andresen D, et al. Catheter ablation for atrial fibrillation with heart failure. *N Engl J Med.* Feb 1 2018;378(5):417-427. PMID 29385358
34. Hakalahti A, Biancari F, Nielsen JC, et al. Radiofrequency ablation vs. antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: systematic review and meta-analysis. *Europace.* Mar 2015;17(3):370378. PMID 25643988
35. Morillo CA, Verma A, Connolly SJ, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation (RAAFT-2): a randomized trial. *JAMA.* Feb 19 2014;311(7):692-700. PMID 24549549
36. Cosedis Nielsen J, Johannessen A, Raatikainen P, et al. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation. *N Engl J Med.* Oct 25 2012;367(17):1587-1595. PMID 23094720

37. Nielsen JC, Johannessen A, Raatikainen P, et al. Long-term efficacy of catheter ablation as first-line therapy for paroxysmal atrial fibrillation: 5-year outcome in a randomised clinical trial. *Heart.* Mar 2017;103(5):368-376. PMID 27566295
38. Zhu M, Zhou X, Cai H, et al. Catheter ablation versus medical rate control for persistent atrial fibrillation in patients with heart failure: A PRISMA-compliant systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore).* Jul 2016;95(30):e4377. PMID 27472728
39. Anselmino M, Matta M, Castagno D, et al. Catheter ablation of atrial fibrillation in chronic heart failure: state-of-the-art and future perspectives. *Europace.* May 2016;18(5):638-647. PMID 26857188
40. Hunter RJ, Berriman TJ, Diab I, et al. A randomized controlled trial of catheter ablation versus medical treatment of atrial fibrillation in heart failure (the CAMTAF trial). *Circ Arrhythm Electrophysiol.* Feb 2014;7(1):31-38. PMID 24382410
41. Jones DG, Haldar SK, Hussain W, et al. A randomized trial to assess catheter ablation versus rate control in the management of persistent atrial fibrillation in heart failure. *J Am Coll Cardiol.* May 7 2013;61(18):1894-1903. PMID 23500267
42. Geng J, Zhang Y, Wang Y, et al. Catheter ablation versus rate control in patients with atrial fibrillation and heart failure: A multicenter study. *Medicine (Baltimore).* Dec 2017;96(49):e9179. PMID 29245366
43. Joy PS, Gopinathannair R, Olshansky B. Effect of ablation for atrial fibrillation on heart failure readmission rates. *Am J Cardiol.* Nov 1 2017;120(9):1572-1577. PMID 28886855
44. Reddy VY, Dukkipati SR, Neuzil P, et al. Randomized, controlled trial of the safety and effectiveness of a contact force-sensing irrigated catheter for ablation of paroxysmal atrial fibrillation: results of the TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (TOCCASTAR) Study. *Circulation.* Sep 8 2015;132(10):907915. PMID 26260733
45. Nakamura K, Naito S, Sasaki T, et al. Randomized comparison of contact force-guided versus conventional circumferential pulmonary vein isolation of atrial fibrillation: prevalence, characteristics, and predictors of electrical reconnections and clinical outcomes. *J Interv Card Electrophysiol.* Dec 2015;44(3):235-245. PMID 26387117
46. Afzal MR, Chatta J, Samanta A, et al. Use of contact force sensing technology during radiofrequency ablation reduces recurrence of atrial fibrillation: A systematic review and meta-analysis. *Heart Rhythm.* Sep 2015;12(9):1990-1996. PMID 26091856
47. Hussein AA, Saliba WI, Martin DO, et al. Natural history and long-term outcomes of ablated atrial fibrillation. *Circ Arrhythm Electrophysiol.* Jun 2011;4(3):271-278. PMID 21493959
48. Teunissen C, Kassenberg W, van der Heijden JF, et al. Five-year efficacy of pulmonary vein antrum isolation as a primary ablation strategy for atrial fibrillation: a single-centre cohort study. *Europace.* Sep 2016;18(9):13351342. PMID 26838694
49. Bunch TJ, May HT, Bair TL, et al. Atrial fibrillation ablation patients have long-term stroke rates similar to patients without atrial fibrillation regardless of CHADS2 score. *Heart Rhythm.* Sep 2013;10(9):1272-1277. PMID 23835257
50. Weerasooriya R, Khairy P, Litalien J, et al. Catheter ablation for atrial fibrillation: are results maintained at 5 years of follow-up? *J Am Coll Cardiol.* Jan 11 2011;57(2):160-166. PMID 21211687
51. Tzou WS, Marchlinski FE, Zado ES, et al. Long-term outcome after successful catheter ablation of atrial fibrillation. *Circ Arrhythm Electrophysiol.* Jun 1 2010;3(3):237-242. PMID 20335557
52. Bertaglia E, Tondo C, De Simone A, et al. Does catheter ablation cure atrial fibrillation? Single-procedure outcome of drug-refractory atrial fibrillation ablation: a 6-year multicentre experience. *Europace.* Feb 2010;12(2):181-187. PMID 19887458
53. Sawhney N, Anousheh R, Chen WC, et al. Five-year outcomes after segmental pulmonary vein isolation for paroxysmal atrial fibrillation. *Am J Cardiol.* Aug 1 2009;104(3):366-372. PMID 19616669
54. Anselmino M, Grossi S, Scaglione M, et al. Long-term results of transcatheter atrial fibrillation ablation in patients with impaired left ventricular systolic function. *J Cardiovasc Electrophysiol.* Jan 2013;24(1):24-32. PMID 23140485
55. Takigawa M, Takahashi A, Kuwahara T, et al. Long-term follow-up after catheter ablation of paroxysmal atrial fibrillation: the incidence of recurrence and progression of atrial fibrillation. *Circ Arrhythm Electrophysiol.* Apr 2014;7(2):267-273. PMID 24610740
56. Chun KR, Schmidt B, Metzner A, et al. The 'single big cryoballoon' technique for acute pulmonary vein isolation in patients with paroxysmal atrial fibrillation: a prospective observational single centre study. *Eur Heart J.* Mar 2009;30(6):699-709. PMID 19109353

57. Paylos JM, Hoyt RH, Ferrero C, et al. Complete pulmonary vein isolation using balloon cryoablation in patients with paroxysmal atrial fibrillation. *Rev Esp Cardiol.* Nov 2009;62(11):1326-1331. PMID 19889345
58. Chen CF, Gao XF, Duan X, et al. Comparison of catheter ablation for paroxysmal atrial fibrillation between cryoballoon and radiofrequency: a meta-analysis. *J Interv Card Electrophysiol.* Apr 2017;48(3):351-366. PMID 28063111
59. Liu XH, Chen CF, Gao XF, et al. Safety and efficacy of different catheter ablations for atrial fibrillation: a systematic review and meta-analysis. *Pacing Clin Electrophysiol.* Aug 2016;39(8):883-899. PMID 27197002
60. Cardoso R, Mendirichaga R, Fernandes G, et al. Cryoballoon versus radiofrequency catheter ablation in atrial fibrillation: a meta-analysis. *J Cardiovasc Electrophysiol.* Oct 2016;27(10):1151-1159. PMID 27422848
61. Buiatti A, von Olshausen G, Barthel P, et al. Cryoballoon vs. radiofrequency ablation for paroxysmal atrial fibrillation: an updated meta-analysis of randomized and observational studies. *Europace.* Mar 01 2017;19(3):378-384. PMID 27702864
62. Cheng X, Hu Q, Zhou C, et al. The long-term efficacy of cryoballoon vs irrigated radiofrequency ablation for the treatment of atrial fibrillation: A meta-analysis. *Int J Cardiol.* Feb 15 2015;181:297-302. PMID 25540844
63. Xu J, Huang Y, Cai H, et al. Is cryoballoon ablation preferable to radiofrequency ablation for treatment of atrial fibrillation by pulmonary vein isolation? A meta-analysis. *PLoS One.* Mar 2014;9(2):e90323. PMID 24587324
64. Andrade JG, Khairy P, Guerra PG, et al. Efficacy and safety of cryoballoon ablation for atrial fibrillation: a systematic review of published studies. *Heart Rhythm.* Sep 2011;8(9):1444-1451. PMID 21457789
65. Packer DL, Kowal RC, Wheelan KR, et al. Cryoballoon ablation of pulmonary veins for paroxysmal atrial fibrillation: first results of the North American Arctic Front (STOP AF) pivotal trial. *J Am Coll Cardiol.* Apr 23 2013;61(16):1713-1723. PMID 23500312
66. Andrade JG, Khairy P, Macle L, et al. Incidence and significance of early recurrences of atrial fibrillation after cryoballoon ablation: insights from the multicenter Sustained Treatment of Paroxysmal Atrial Fibrillation (STOP AF) Trial. *Circ Arrhythm Electrophysiol.* Feb 2014;7(1):69-75. PMID 24446022
67. Kuck KH, Brugada J, Furnkranz A, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. *N Engl J Med.* Jun 09 2016;374(23):2235-2245. PMID 27042964
68. Kuck KH, Furnkranz A, Chun KR, et al. Cryoballoon or radiofrequency ablation for symptomatic paroxysmal atrial fibrillation: reintervention, rehospitalization, and quality-of-life outcomes in the FIRE AND ICE trial. *Eur Heart J.* Oct 07 2016;37(38):2858-2865. PMID 27381589
69. Luik A, Radzewitz A, Kieser M, et al. Cryoballoon versus open irrigated radiofrequency ablation in patients with paroxysmal atrial fibrillation: the prospective, randomized, controlled, noninferiority FreezeAF Study. *Circulation.* Oct 6 2015;132(14):1311-1319. PMID 26283655
70. Hunter RJ, Baker V, Finlay MC, et al. Point-by-point radiofrequency ablation versus the cryoballoon or a novel combined approach: a randomized trial comparing 3 methods of pulmonary vein isolation for paroxysmal atrial fibrillation (The Cryo Versus RF Trial). *J Cardiovasc Electrophysiol.* Dec 2015;26(12):1307-1314. PMID 26727045
71. Koch L, Haeusler KG, Herm J, et al. Mesh ablator vs. cryoballoon pulmonary vein ablation of symptomatic paroxysmal atrial fibrillation: results of the MACPAF study. *Europace.* Oct 2012;14(10):1441-1449. PMID 22523379
72. Malmborg H, Lonnerholm S, Blomstrom P, et al. Ablation of atrial fibrillation with cryoballoon or duty-cycled radiofrequency pulmonary vein ablation catheter: a randomized controlled study comparing the clinical outcome and safety; the AF-COR study. *Europace.* Nov 2013;15(11):1567-1573. PMID 23703361
73. Neumann T, Vogt J, Schumacher B, et al. Circumferential pulmonary vein isolation with the cryoballoon technique results from a prospective 3-center study. *J Am Coll Cardiol.* Jul 22 2008;52(4):273-278. PMID 18634982
74. Linhart M, Bellmann B, Mittmann-Braun E, et al. Comparison of cryoballoon and radiofrequency ablation of pulmonary veins in 40 patients with paroxysmal atrial fibrillation: a case-control study. *J Cardiovasc Electrophysiol.* Dec 2009;20(12):1343-1348. PMID 19656254

75. Abugattas JP, Iacopino S, Moran D, et al. Efficacy and safety of the second generation cryoballoon ablation for the treatment of paroxysmal atrial fibrillation in patients over 75 years: a comparison with a younger cohort. *Europace.* Nov 1 2017;19(11):1798-1803. PMID 28402529
76. Aryana A, Singh SM, Kowalski M, et al. Acute and long-term outcomes of catheter ablation of atrial fibrillation using the second-generation cryoballoon versus open-irrigated radiofrequency: a multicenter experience. *J Cardiovasc Electrophysiol.* Aug 2015;26(8):832-839. PMID 25917655
77. Schmidt M, Dorwarth U, Andresen D, et al. Cryoballoon versus RF Ablation in paroxysmal atrial fibrillation: results from the German Ablation Registry. *J Cardiovasc Electrophysiol.* Jan 2014;25(1):1-7. PMID 24134539
78. Schmidt M, Dorwarth U, Andresen D, et al. German ablation registry: Cryoballoon vs radiofrequency ablation in paroxysmal atrial fibrillation-One-year outcome data. *Heart Rhythm.* Apr 2016;13(4):836-844. PMID 26681608
79. Su W, Orme GJ, Hoyt R, et al. Retrospective review of Arctic Front Advance Cryoballoon Ablation: a multicenter examination of second-generation cryoballoon (RADICOOL trial). *J Interv Card Electrophysiol.* Apr 2018;51(3):199-204. PMID 29478173
80. Jourda F, Providencia R, Marijon E, et al. Contact-force guided radiofrequency vs. second-generation balloon cryotherapy for pulmonary vein isolation in patients with paroxysmal atrial fibrillation-a prospective evaluation. *Europace.* Feb 2015;17(2):225-231. PMID 25186456
81. Squara F, Zhao A, Marijon E, et al. Comparison between radiofrequency with contact force-sensing and second-generation cryoballoon for paroxysmal atrial fibrillation catheter ablation: a multicentre European evaluation. *Europace.* May 2015;17(5):718-724. PMID 25840289
82. Julia J, Chierchia GB, de Asmundis C, et al. Regular atrial tachycardias following pulmonary vein isolation for paroxysmal atrial fibrillation: a retrospective comparison between the cryoballoon and conventional focal tip radiofrequency techniques. *J Interv Card Electrophysiol.* Mar 2015;42(2):161-169. PMID 25597847
83. Wasserlauf J, Pelchovitz DJ, Rhyner J, et al. Cryoballoon versus radiofrequency catheter ablation for paroxysmal atrial fibrillation. *Pacing Clin Electrophysiol.* Apr 2015;38(4):483-489. PMID 25627795
84. Linhart M, Nielson A, Andrie RP, et al. Fluoroscopy of spontaneous breathing is more sensitive than phrenic nerve stimulation for detection of right phrenic nerve injury during cryoballoon ablation of atrial fibrillation. *J Cardiovasc Electrophysiol.* Aug 2014;25(8):859-865. PMID 24724724
85. Lakhani M, Saiful F, Parikh V, et al. Recordings of diaphragmatic electromyograms during cryoballoon ablation for atrial fibrillation accurately predict phrenic nerve injury. *Heart Rhythm.* Mar 2014;11(3):369-374. PMID 24252287
86. Vogt J, Heintze J, Gutleben KJ, et al. Long-term outcomes after cryoballoon pulmonary vein isolation: results from a prospective study in 605 patients. *J Am Coll Cardiol.* Apr 23 2013;61(16):1707-1712. PMID 23199518
87. Neumann T, Wojcik M, Berkowitsch A, et al. Cryoballoon ablation of paroxysmal atrial fibrillation: 5-year outcome after single procedure and predictors of success. *Europace.* Aug 2013;15(8):1143-1149. PMID 23419659
88. Boho A, Misikova S, Spurny P, et al. A long-term evaluation of cryoballoon ablation in 205 atrial fibrillation patients: a single center experience. *Wien Klin Wochenschr.* Oct 2015;127(19-20):779-785. PMID 26142169
89. Davies AJ, Jackson N, Barlow M, et al. Long term follow-up of pulmonary vein isolation using cryoballoon ablation. *Heart Lung Circ.* Mar 2016;25(3):290-295. PMID 26621109
90. Dukkipati SR, Cuoco F, Kutinsky I, et al. Pulmonary vein isolation using the visually guided laser balloon: a prospective, multicenter, and randomized comparison to standard radiofrequency ablation. *J Am Coll Cardiol.* Sep 22 2015;66(12):1350-1360. PMID 26383722
91. Schmidt B, Neuzil P, Luik A, et al. Laser balloon or wide-area circumferential irrigated radiofrequency ablation for persistent atrial fibrillation: a multicenter prospective randomized study. *Circ Arrhythm Electrophysiol.* Dec 2017;10(12). PMID 29217521
92. Lellouche N, Jais P, Nault I, et al. Early recurrences after atrial fibrillation ablation: prognostic value and effect of early reablation. *J Cardiovasc Electrophysiol.* Jun 2008;19(6):599-605. PMID 18462321
93. Pokushalov E, Romanov A, De Melis M, et al. Progression of atrial fibrillation after a failed initial ablation procedure in patients with paroxysmal atrial fibrillation: a randomized comparison of drug therapy versus reablation. *Circ Arrhythm Electrophysiol.* Aug 2013;6(4):754-760. PMID 23748210
94. Gupta A, Perera T, Ganesan A, et al. Complications of catheter ablation of atrial fibrillation: a systematic review. *Circ Arrhythm Electrophysiol.* Dec 1 2013;6(6):1082-1088. PMID 24243785

95. Shah RU, Freeman JV, Shilane D, et al. Procedural complications, rehospitalizations, and repeat procedures after catheter ablation for atrial fibrillation. *J Am Coll Cardiol.* Jan 10 2012;59(2):143-149. PMID 22222078
96. Dagres N, Hindricks G, Kottkamp H, et al. Complications of atrial fibrillation ablation in a high-volume center in 1,000 procedures: still cause for concern? *J Cardiovasc Electrophysiol.* Sep 2009;20(9):1014-1019. PMID 19490383
97. Waldo AL, Wilber DJ, Marchlinski FE, et al. Safety of the open-irrigated ablation catheter for radiofrequency ablation: safety analysis from six clinical studies. *Pacing Clin Electrophysiol.* Sep 2012;35(9):1081-1089. PMID 22817524
98. Ellis ER, Culler SD, Simon AW, et al. Trends in utilization and complications of catheter ablation for atrial fibrillation in Medicare beneficiaries. *Heart Rhythm.* Sep 2009;6(9):1267-1273. PMID 19716081
99. Cappato R, Calkins H, Chen SA, et al. Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. *J Am Coll Cardiol.* May 12 2009;53(19):1798-1803. PMID 19422987
100. Haeusler KG, Koch L, Herm J, et al. 3 Tesla MRI-detected brain lesions after pulmonary vein isolation for atrial fibrillation: results of the MACPAF study. *J Cardiovasc Electrophysiol.* Jan 2013;24(1):14-21. PMID 22913568
101. Herm J, Fiebach JB, Koch L, et al. Neuropsychological effects of MRI-detected brain lesions after left atrial catheter ablation for atrial fibrillation: long-term results of the MACPAF study. *Circ Arrhythm Electrophysiol.* Oct 2013;6(5):843-850. PMID 23989301
102. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society. *Heart Rhythm.* Apr 2012;9(4):632-696 e621. PMID 22386883
103. 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 1 2018;20(1):e1-e160. PMID 29016840
104. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol.* Dec 02 2014;64(21):e1-76. PMID 24685669
105. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace.* Nov 2016;18(11):1609-1678. PMID 27567465