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Atrial fibrillation - Who Needs Catheter Ablation And Which Approach?

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Abstract

Catheter ablation therapy for atrial fibrillation (AF) has gained a significant role during maintenance of sinus rhythm compared to antiarrhythmic medication. Catheter ablation techniques are also improved and progressed over years in parallel to better understanding of disease mechanisms and technological advancements. However, due to invasive nature of the therapy with its pertinent procedural risks, both appropriate patient selection and use of relevant approach should be considered by all electrophysiologists before decide to perform catheter ablation.

Introduction

Atrial fibrillation (AF) affects approximately 30 million individuals worldwide and is known as a major cause of stroke, heart failure, hospitalizations and death.[1] The recognition for the first time that, in a subset of patients, AF was triggered by a rapidly firing focus and could be "cured" with a localized ablation procedure eventually led to the progressive innovations in catheter ablation technologies.[2] Percutaneous catheter ablation is now an evidenced and established therapeutic option for rhythm control in selected AF patients with reasonable safety and efficacy.[3] However, success rates for persistent AF ablation still remain far lower than paroxysmal AF, despite a large spectrum of ablation strategies.[3] Therefore, appropriate AF patient selection with relevant catheter ablation technique should be considered by all electrophysiologists during treatment of AF via rhythm control strategy.

This review addresses current approaches in the field of catheter ablation for AF.

Why Ablation?

A number of systematic reviews have been performed to evaluate the efficacy of catheter ablation versus antiarrhythmic drug therapy for AF.[4-6] The efficacy of radiofrequency catheter ablation for maintaining sinus rhythm (SR) has been found to be superior to current antiarrhythmic drug therapy for providing freedom from symptomatic AF and improving quality of life in selected patient populations.[7-9] Studies have also demonstrated a reduction of AF-related symptoms.[10] However, evidence is insufficient to determine whether catheter ablation reduces all-cause mortality, stroke, or heart failure (HF).

Evidence supporting the efficacy of catheter ablation is strongest for paroxysmal AF in younger patients with little or no structural heart disease.[11]

Who to Ablate?

First, reversible causes of AF should be investigated thoroughly prior to giving consideration to catheter ablation. These include evaluation for hyperthyroidism, pulmonary embolism, myocardial ischemia/infarction, heavy alcohol consumption, recent cardiac surgery and other acute inflammatory/infectious processes. Supraventricular arrhythmias, such as atrioventricular (AV) nodal reentry, AV reentry tachycardia, or atrial tachycardia may also serve as triggers for AF, therefore eliminating those supraventricular tachycardia episodes may help limit or eliminate episodes of AF.

Beyond these, determining whether a patient is an appropriate candidate for catheter ablation depends on various factors, including the type of AF (paroxysmal, persistent, or long-standing persistent), severity of symptoms, presence of structural heart disease, candidacy for alternative options such as rate control or antiarrhythmic drug therapy, likelihood of complications, and patient preference.[3] When patient preference is excluded, the primary selection criterion for catheter ablation should be the presence of symptomatic AF.[3]

ACC/AHA guidelines[11] have stated that AF catheter ablation:

a) Is useful for symptomatic paroxysmal AF [Class I, level of evidence (LOE): A];

b) Is reasonable for selected patients with symptomatic persistent

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AF (Class IIa, LOE: A);

c) May be considered for symptomatic long-standing (>12 months) persistent AF (Class IIb, LOE: B) refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm control strategy is desired.

The difference in recommendations of HRS/EHRA/ECAS guidelines[3] from ACC/AHA guidelines is that AF catheter ablation is reasonable for selected patients with symptomatic persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication with Class IIa, LOE: B indication.

ESC guidelines[12] have recommended catheter ablation of symptomatic paroxysmal AF in patients who have symptomatic recurrences of AF on antiarrhythmic drug therapy and who prefer further rhythm control therapy (Class I, LOE: A). They have also stated that catheter ablation of AF should be considered as first-line therapy in selected patients with symptomatic paroxysmal AF as an alternative to antiarrhythmic drug therapy, considering patient choice, benefit, and risk (Class IIa, LOE: B).[12] HRS/EHRA/ECAS guideline[3] have additionally mentioned that catheter ablation as first-line therapy could be considered in persistent AF (Class IIb, LOE: C) and might be considered in long-standing persistent AF patients (Class IIb, LOE: C).

It is not recommended to perform catheter ablation for AF in patients who cannot receive anticoagulant therapy during and following the procedure (Class III, LOE: C).[11]

At last but not least, when catheter ablation is found appropriate for a patient, some patient characteristics that are known to increase the incidence and burden of AF should be corrected prior to catheter ablation to improve procedural outcomes. For instance, recent studies have demonstrated the importance of weight loss and sleep apnea treatment prior to ablation.[13]

Catheter Ablation in Special Patient Populations

The safety and efficacy of catheter ablation are less well established for some populations of patients, especially very elderly patients, and patients with significant HF.[3]

In Patients with HF

Restoring sinus rhythm has a positive impact on heart failure as atrial contraction and AV synchrony are important contributors to total cardiac output. In patients who suffer from symptomatic AF recurrences on amiodarone therapy, catheter ablation remains as the sole choice for escalated rhythm control therapy. It is indicated to improve AF-related symptoms (EHRA score II–IV).[12]

Studies evaluating the role of catheter ablation for AF in HF patients have demonstrated an acceptable rate of successful sinus rhythm maintenance with improvements in left ventricular ejection fraction (LVEF) and symptoms.[14-16] Therefore, most clinicians reserve AV node ablation/biventricular pacing for elderly patients, patients with significant comorbidities who would not tolerate catheter ablation for AF, or patients with preexisting biventricular implantable cardioverter defibrillators and AF with ventricular response rates rapid enough to limit the amount of biventricular pacing.

The degree of LVEF improvement varies according to patient characteristics.[17] For instance, where the LV dysfunction is thought to be due to AF itself, AF catheter ablation and maintenance of sinus rhythm may result in a marked improvement. Improved rate control or cardioversion with antiarrhythmic drug therapy may help predict the outcomes of catheter ablation in such cases. On the other hand, in patients with HF who develop AF, a rhythm-control strategy is not superior to a rate-control strategy.[18]

Due to the extent of remodeling and underlying heart disease, recurrence[19] and complication rates are higher in this population. A meta-analysis had reported that the single-procedure efficacy of AF catheter ablation was lower in patients with systolic dysfunction, but a similar success rate could be achieved among patients with and without systolic dysfunction with repeat procedures.[20] Recently, in a study including 81 patients with LVEF≤45%, Rillig et al.[21] showed that single-procedure success rates after PVI during 6 years of follow-up were low (35.1%). In patients with single- or multiple-procedure ablation success, a higher improvement of LVEF was observed. Another long-term follow-up study has shown that at 5 years, 60.7% of patients with systolic heart failure had clinical recurrence of AF.[22] In a systematic review[23] including 26 randomized controlled trials, clinical trials, and observational studies of patients with left ventricular systolic dysfunction undergoing catheter ablation for AF, efficacy in maintaining sinus rhythm at a mean follow-up of 23 months was found to be 60%. Left ventricular ejection fraction significantly improved during follow-up by 13%. A recent meta-analysis of 4 trials (n=224) which randomized HF patients (LVEF<50%) with persistent AF to a rate control or AF catheter ablation strategy, AF catheter ablation has been reported to be superior to rate control in improving LVEF, quality of life and functional capacity.[24]

Other than systolic heart failure, severe diastolic left ventricular dysfunction has also been shown to result in a higher risk of AF recurrence after catheter ablation.[25]

Elderly Patients

Age was shown to be an independent predictor of AF recurrence following catheter ablation for AF.[26] Hsieh et al.[27] compared outcomes after catheter ablation for AF and AV node ablation in 71 patients >65 years at a mean follow-up of 52 months. Patients who had ablation of AF were more likely to have symptomatic AF, less persistent AF, better New York Heart Association functional class and less heart failure than the patients who underwent AV node ablation. However, the prevalence of stroke, mortality and other complications were similar between the AF ablation and AV node ablation groups. Corrado et al.[28] showed that catheter ablation for AF in 174 patients older than 75 years resulted in a clinical efficacy of 73 and 80% after single and repeat ablation procedures, respectively at a mean follow-up of 22 months. Zado et al.[29] also compared the safety and efficacy of catheter ablation in three groups of patients: <65, 65-74, and ≥75 years over a 27 month follow-up period. Patients over the age of 75 were more likely to demonstrate a partial response to ablation and require antiarrhythmic drug therapy. Another study had stratified 1548 patients who underwent AF ablation according to age <45, 45–54, 55–64 and ≥65 years. Outcomes, defined as rare or no AF with or without antiarrhythmic drugs, were similar in all groups with an 82–88% success rate.[30] In another study, 35 octogenarians undergoing AF ablation were compared to 717 younger patients also undergoing RF ablation. They found similar success rates of 78 and 75%, respectively.[31] Another study looked prospectively at 103 octogenarians compared with 2651 younger patients, and found 69% of octogenarians were free of AF compared with 71% of their younger peers.[32] However, both Spragg et al.[33] and Shah et al.[34] reported that older age has been significantly associated with a higher risk of complications, suggesting careful assessment of the risk/benefit profile in

these patients before catheter ablation for AF.

Patients With Hypertrophic Cardiomyopathy (HCM)

ACC/ AHA guidelines[11] have stated that AF catheter ablation can be beneficial in patients with HCM in whom a rhythm-control strategy is desired when antiarrhythmic drugs fail or are not tolerated (class IIa, LOE: B). Contreras-Valdes et al.[35] have compared long-term arrhythmia control among patients with HCM and a non-affected cohort and found that the efficacy of AF ablation is significantly lower compared with non-affected patients, irrespective of the number of procedures or use of antiarrhythmic drugs and when present, left ventricular outflow obstruction could be a strong predictor of recurrence. Gaita et al.[36] have demonstrated that 64% of 24 AF patients with HCM had AF-free survival at a mean follow-up of 19 months following catheter ablation. Similarly, Bunch et al.[37] have shown that 1 year AF-free survival was 62% in 33 patients with HCM. Okamatsu et al.[38] have reported that during a mean follow-up of 21 months, sinus rhythm was maintained in 59% of HCM patients who underwent catheter ablation for AF. On the other hand, Bassiouny et al.[39] have reported that only 29% of HCM patients who underwent catheter ablation had no documented recurrent atrial arrhythmia after a single procedure after a follow-up of 35 months.

Patients with Mechanical Mitral Valve (MMV)

Previous studies have demonstrated that catheter ablation of AF in patients with MMV is feasible and safe but is associated with higher recurrence than in patients with native valve.[40-43] Lakkireddy et al.[42] have shown that at 12 months, 80% of patients in the mitral or aortic prosthetic valve group were in sinus rhythm after an average of 1.3 procedures. Hussein et al.[43] have reported that of 81 patients with MVR, 56 (69.1%) were arrhythmia free while not taking antiarrhythmic drugs, 11 (13.6%) had their arrhythmia controlled with antiarrhythmic drugs that had previously failed, and 14 (17.3%) had drug-resistant AF and were managed with rate control. In this study, all MMV patients underwent ablation under therapeutic international normalized ratio. No entrapment of catheters or stroke had occurred and there were no differences in terms of procedure-related complications between the groups.

A recent study has compared the efficacy and long-term outcome of pulmonary vein (PV) antrum isolation (PVAI) alone versus extended PVAI plus non-PV trigger elimination for the treatment of AF in patients with MMV.[44] It was found that compared with the standard PVAI alone, a strategy including extended PVAI and non-PV trigger elimination was associated with a higher 12-month and long-term arrhythmia-free survival in patients with MMV undergoing AF ablation. Very late recurrence occurred in up to 18.8% of patients undergoing extensive ablation, with focal AT being the most common type of recurrent arrhythmia.

Athletes

ACC/AHA guidelines[11] state that radiofrequency (RF) catheter ablation (RFCA) can be considered in athletes with AF episodes.[45]

Re-Ablation

Recovery of PV conduction may necessitate re-ablation in certain patients.[46] Patients with persistent AF are more likely to need a repeat ablation than those with paroxysmal AF.[47] Current guidelines do not specify when re-ablation should be performed; however, it is generally recommended to withhold repeat procedures for a 3-month period after the first procedure as residual areas of conduction in the PVs may take time to become clinically apparent.[3]

Other

Recent studies have demonstrated that severity of atrial fibrosis was associated with decreased response to catheter ablation.[48-51] The tissue characterization of the LA wall regarding atrial fibrosis on DE-MRI was found to be correlated with electroanatomic voltage mapping (EAVM).[49] Relying on this, identification and acute targeting of gaps in atrial ablation lesions sets have been investigated using a real-time MRI system.[52,53] Major limitation is that this modality requires extensive MRI experience, and its reproducibility is still under investigation.

Approaches in AF Ablation

The early percutaneous catheter ablation procedures were designed to mimic a surgical Cox maze procedure, which was based on the 'multiple wavelet hypothesis' for AF. This hypothesis suggested that, as long as the atrium had a sufficient area with adequately short refractory periods, AF could be initiated and then indefinitely perpetuated. Therefore, the early attempts at interventional AF treatment aimed to decrease arrhythmia perpetuation by compartmentalizing the atrium into smaller regions incapable of sustaining the critical number of circulating wavelets.

Today, the most common goal, particularly for ablation of paroxysmal AF in younger patients whose atria have undergone little or no atrial remodelling, is complete PV isolation (PVI) with unidirectional or bidirectional conduction block. PVI alone is much less successful for AF control dominated by "substrate" (persistent and long-standing persistent AF) when there has been extensive and irreversible atrial remodelling. In such cases, some other strategies including successful isolation of sites of non-PV triggers; elimination of sites harboring complex fractionated atrial electrograms (CFAE); linear ablation with bidirectional block; ablation of sites harboring ganglionated plexi (GP); ablation utilizing electrogram analysis to eliminate sites of AF rotors or other drivers; ablation with a goal of conversion to SR during ablation; or ablation until the absence of any atrial arrhythmias during attempts at re-induction must be considered.

Following PVI, data supporting the use of any particular strategy over another for improved long-term clinical outcomes is inconsistent and adjunctive strategies to PVI are often selected based on operator experience and preference.[54-57] Heterogeneity between patient populations may be explanatory to explain the variation in the results of outcome studies. Besides, the different end-points, follow-up periods and protocols often limit comparisons of studies (Also see "Success rates of AF ablation").

Ablation Approaches Targeting PVs

Rapidly firing foci initiating paroxysmal AF arise most commonly from LA myocardial sleeves that extend into the PVs.[2] These observations led to the development of segmental PVI as the cornerstone for ablation strategies.[58] An ablation strategy of encircling the PVs with RF lesions guided by 3D electroanatomical mapping was subsequently developed by Pappone et al.[59] Strategies then shifted to target the atrial tissue located in the antrum rather than the PV itself ("segmental PV ablation" or "wide area circumferential ablation") following the recognition of both PV stenosis as a complication of RF delivery within a PV, or the PV antrum. And today, circumferential isolation of PVs has become the standard therapy for paroxysmal AF.

Most clinicians have identified their primary endpoint for PV ablation as the elimination (or dissociation) of the PV potentials re-

corded from a circular multipolar electrode catheter. 10% rely on exit block as an endpoint for the ablation procedure.[3]

Ablation Approaches not Targeting PVs

Additive strategies to PVI have been sought, particularly in persistent and long- standing persistent AF patients, to improve outcomes of catheter ablation.

Linear Ablation

The rationale underlying creating linear LA lesions[60] originates from the surgical Cox maze procedure, and follows the 'multiple wavelet hypothesis' that postulates that compartmentalizing the LA into smaller regions incapable of sustaining micro re-entry will improve outcomes. Added benefits include the potential effect on the macro re-entrant tachycardias that can occur post-AF ablation.

Unfortunately, achievement of complete conduction block across linear lesions can be very difficult to achieve since the lesions have to be both contiguous and transmural. Thus, whereas complete lines may prevent recurrent arrhythmias, if incomplete they may be proarrhythmic and result in higher prevalence of LA flutter.[61] Therefore, the addition of linear lesions confers no benefit when compared to PVI alone in paroxysmal AF patients.[56,62] A slight advantage has been suggested in persistent AF patients where two small, randomized trials have demonstrated a significant benefit.[62,63] However, the recent Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial Part II trial (STAR- AF II) has failed to show any beneficial effect of linear ablation in addition to PVI in persistent AF patients.[57]

Non-PV Triggers

The sites of origin for non-PV atrial triggers include the posterior wall of the LA, the superior vena cava, the inferior vena cava, the crista terminalis, the fossa ovalis, the coronary sinus, behind the Eustachian ridge, along the ligament of Marshall, and adjacent to the AV valve annuli.[64] Furthermore, re-entrant circuits maintaining AF may be located within the right and left atria. In selected patients, elimination of only the non-PV triggers has resulted in elimination of AF.[65,66]

Ablation of CFAES

Complex fractionated atrial electrograms are regarded to represent areas of slow conduction, conduction block, or 'pivot' points for a local AF perpetuating re-entry. The primary endpoints during RF ablation of AF using this approach are either complete elimination of the areas with CFAEs, conversion of AF to sinus rhythm, and/or non- inducibility of AF. For patients with paroxysmal AF, the endpoint of the ablation procedure using this approach is non- inducibility of AF. For patients with persistent AF, the endpoint of ablation with this approach is AF termination. Similar to linear lesion, studies have demonstrated that CFAE ablation as a lone ablation strategy is inadequate for both paroxysmal and persistent AF.[67,68] Likewise, in the paroxysmal AF population there appears to be limited benefit for adjunctive CFAE ablation.[62,67,69,70] In those with persistent AF, observational and randomized studies have demonstrated that ablation of CFAE areas, in addition to PVI, improves the procedural outcome.[62,67,71,72] Recent STAR- AF II trial, on the other hand, has failed to demonstrate any beneficial effect of CFAE ablation in addition to PVI in persistent AF patients.[57] One of the limitations of targeting CFAEs with ablation has been the extensive amount of ablation needed. Half of the clinicians have stated that they routinely employed CFAE-based ablation as part of an initial ablation procedure in patients with long-standing persistent AF.[3]

Ablation Of GPs

Adding GPs to other ablation targets has been shown to improve ablation success.[73,74]

Other Unestablished Ablation Strategies

A) Voltage Map-Guided Substrate Modification: Box Isolation Of Fibrotic Areas (BIFA)

The regional localization and the extent of the fibrotic LA substrate can be visualized during the intervention in sinus rhythm applying EAVM; this allows the use of a new patient-tailored ablation strategy, BIFA, for the circumferential isolation of the significantly affected fibrotic areas (e.g., <0.5 mV). An individualized substrate modification using BIFAs may be added to circumferential PVI in patients with paroxysmal AF, or who have very substantial regional LA fibrosis detected in the first ablation session. However, in patients with massive fibrosis, failure of the initial ablation is likely regardless of the applied ablation concept, and further ablation procedures should be discouraged and avoided.

There are several limitations of methods for identifying substrates. Voltage maps using point-by-point mapping not only take time, but the measured voltage also depends on the rhythm (sinus, atrial fibrillation, atrial extrasystole), the electrode contact with tissue, and the atrial myocardium thickness. Therefore, clear limits or definitions for a normal voltage (e.g., >1.5mV, >2.0mV) and a highly abnormal voltage (e.g., <0.5 mV) do not exist.

B) Focal Impulse and Rotor Modulation (FIRM)

The follow-up results of FIRM strategy, in which a 64-pole basket catheter is advanced into the left and right atria to demonstrate focal impulse and rotors, have revealed that patients who underwent FIRM-guided ablation maintained higher freedom from AF versus those who underwent conventional ablation.[75] AF sources were analyzed to be co- incidentally ablated in 45% of conventional cases.[76] These results were also confirmed in a multicenter study.[43]

Ensuring Durable Isolation

Various techniques have been proposed to identify regions of incomplete ablation and/or residual gaps within the index ablation line. One technique is the use of intravenous adenosine to differentiate permanent PV-atrial block from dormant conduction. Not all studies have been in agreement concerning adenosine application.[77-81] Results of Adenosine Following Pulmonary Vein Isolation to Target Dormant Conduction Elimination [ADVICE] trial has recently been published,[82] supporting that adenosine administration should be considered for incorporation into routine clinical practice. An alternative strategy is the 'pace-capture guided' approach, where, after completion of PVI, the antral ablation line encircling the ipsilateral PVs is mapped while pacing from the ablation catheters distal electrode pair.[83,84] Where local LA capture is identified, additional ablation can be performed with the goal of closure of the residual gaps. And also, to attain durable PVI, waiting time after PVI is also important. In a study, Yamane et al.[85] demonstrated that provocation and elimination of time- and ATP-induced early PV re-connection is recommended not only at 30 minutes but also at 60 minutes after PVI to improve its efficacy.

Energy Sources

Radiofrequency energy is by far the dominant energy source that has been used for catheter ablation of AF. RF energy achieves myocardial ablation by the conduction of alternating electrical current through myocardial tissue. The tissue resistivity results in distribution

of RF energy as heat, and the heat then conducts passively to deeper tissue layers. Most tissues exposed to temperatures of 50°C or higher for more than several seconds will show irreversible coagulation necrosis, and evolve into non-conducting myocardial scar. High power delivery and good electrode–tissue contact promote the formation of larger lesions and improve procedure efficacy. Most clinicians employ irrigated tip catheters for delivering RF energy.[3] Comparative trials of irrigated tip and large tip RF technologies versus conventional RF electrodes have demonstrated increased efficacy and decreased procedure duration in the ablation of AFlu,[86,87] but only limited trials of large tip and open irrigation catheters have been performed in patients undergoing AF ablation.

Cryoablation has more recently been developed as a tool for AF ablation procedures. Cryoablation systems work by delivering liquid nitrous oxide under pressure through the catheter to its tip or within the balloon, where it changes to gas, resulting in cooling of surrounding tissue. This gas is then carried back through the reciprocating vacuum lumen. The mechanism of tissue injury results from tissue freezing with a creation of ice crystals within the cell that disrupts cell membranes and interrupts both cellular metabolism and any electrical activity in that cell. In addition, interruption of microvascular perfusion may interrupt blood flow, similarly producing cell death. Complete vein occlusion is required for the creation of circumferential PV lesions and electrical PVI using the cryoballoon ablation catheter.[88]

The reported complications related to catheter ablation of AF may include vascular access complications such as hematoma, retroperitoneal bleeding, pseudoaneurysm, arteriovenous fistula; myocardial perforation and pericardial tamponade; pulmonary vein stenosis; phrenic nerve palsy; thromboembolic events including transient ischemic attacks and stroke; atrioesophageal fistula; and death.

Cryoablation is known to cause less patient discomfort and require lower doses of conscious sedation when compared with RFCA. It also carries a low risk of thrombus formation[89] and therefore, a decreased risk of embolization and stroke. Cryoenergy leaves the connective tissue matrix intact and theoretically, is less likely to lead to myocardial perforation and tamponade compared with RFCA. However, a recent study of 133 consecutive patients undergoing AF ablation has found a similar incidence of pericardial effusions between those treated with cryoballoon ablation and radiofrequency ablation.[90] Otherwise, both procedures have similar risks of injury of adjacent structures (esophagus, phrenic nerves, vagus nerves, lung parenchyma). Although ostial cryoablation reduced the incidence of PV stenosis significantly, the risk still has not been eliminated. Despite animal models showing greater risk of PV stenosis with RFCA[91] and lack of evidence of collagen deposition or PV stenosis 3 months post-cryoablation,[92] PV stenosis may also complicate cryoablation. Clinical data from a small series have shown esophageal ulcerations with cryoablation, but no progression to fistula.[93]

Although point-by-point RF energy and cryoballoon ablation are the two standard ablation systems used for catheter ablation of AF today, balloon-based ultrasound ablation,[94] and laser based ablation systems[95] also have been developed for AF ablation.

Novelties In Ablation

Multielectrode Circumferential Ablation Catheters

The principal purpose of the multielectrode circular ablation catheter systems is to provide ablation and mapping on a single platform.[96,97] The PV ablation catheter (PVAC, Medtronic Ablation Frontiers, Carlsbad, CA) is a 9F deflectable circular multi-electrode catheter that enables mapping and circumferential PV ablation. The latter is the irrigated multi-electrode nMARQ ablation system (Biosense Webster, Inc., Diamond Bar, CA, USA), which allows multi-electrode ablation. The key difference in the nMARQ system is its integration into the CARTO3 platform (Biosense Webster, Inc., Diamond Bar, CA, USA) allowing full visualization of the catheter loop and electrodes, as well as the fact that the catheter is irrigated with 10 irrigation holes per electrode (completely surrounding the electrodes). Recently, multicenter registries including patients referred for paroxysmal or persistent AF underwent PVI by the nMARQ ablation system have shown high acute success rates and shorter procedural times.[98,99] However, several recent studies have reported a higher incidence of silent microemboli following ablation with a multielectrode ablation catheter.[100,101]

Electroanatomic Mapping Systems

Electroanatomic mapping systems combine anatomic and electrical information by a catheter point-by-point mapping, allowing an accurate 3D anatomic reconstruction of the targeted cardiac chamber. There are two different electroanatomic mapping systems that are widely used in clinical practice. The current generation of the CARTO mapping system (CARTO-3, Biosense Webster, Diamond Bar, CA, USA) relies on both a magnet-based localization for visualization of the ablation catheter and an impedance-based system that allows for both tip and catheter curve visualization as well as simultaneous visualization of multiple electrodes.[102] The second electroanatomic mapping system is an electrical impedance mapping system (NavX, St. Jude Medical Inc., Minneapolis, MN, USA) using voltage and impedance for localization.[103] The use of these 3D mapping systems has been demonstrated to reduce fluoroscopy duration.[102,103] To further improve anatomic accuracy of the maps, the 3D images may be integrated with computed tomography (CT) or magnetic resonance imaging (MRI).[104] However, it should not be forgotten that CT or MRI images are not real-time images, and that the accuracy of image integration is dependent on the accuracy of the image fusion. Furthermore, another potential limitation of electroanatomic mapping is the relatively static nature of the geometry, which may need to be updated during the procedure because of changes in anatomy (volume status and tissue edema) or if the location reference has moved. The development of 3D intracardiac echo (ICE) probes may overcome the limitations in geometry creation as one could navigate the real-time 3D image. It has been demonstrated that RFCA of paroxysmal AF using the CARTO 3 system and ICE could be performed safely without fluoroscopy.[105]

Overall, studies on the use of mapping systems on safety and efficacy of AF ablation have revealed contradictory results.[106-108] Most clinicians prefer using these systems when performing AF ablation excluding cases where a balloon-based ablation system is used.[3]

Special Issues in Catheter Ablation

It has been shown that RFCA of AF performed under therapeutic international normalized ratio (INR) does not increase bleeding risk and reduces the risk of emboli.[109,110] Although in guidelines, it is recommended to use novel oral anticoagulant agents with caution for patients undergoing catheter ablation because of the lack of approved antidotes in the event of cardiac tamponade,[11] recently in Active-controlled multi-center study with blind-adjudication designed to evaluate the safety of uninterrupted Rivaroxaban and uninterrupted vitamin K antagonists in subjects undergoing cathEter

ablation for non-valvular Atrial Fibrillation (VENTURE- AF) trial, it has been shown that the use of uninterrupted oral rivaroxaban was feasible and event rates were similar to those for uninterrupted VKA therapy.[111]

Periprocedural protamine administration following catheter ablation to reverse heparin- mediated effects have been shown to allow quicker sheath removal and minimize the risk of potential vascular complications without causing an increase in thrombotic events.[112-114]

Success Rates Of AF Abalation

A meta-analysis of 4 prospective, randomized clinical trials reported that 76% of patients treated with catheter ablation were free of AF compared with 19% of patients randomized to antiarrhythmic drugs.[115] Another meta-analysis involving 63 AF ablation studies reported that the single-procedure success of ablation with no antiarrhythmic drug therapy was 57%, the multiple-procedure success rate with no antiarrhythmic drug therapy was 71%, and the multiple procedure success rate with antiarrhythmic drugs was 77%. In comparison, the success rate for antiarrhythmic drug therapy was 52%.[6]

Medical Antiarrhythmic Treatment or Radiofrequency Ablation in Paroxysmal Atrial Fibrillation (MANTRA-PAF) trial[116] compared first-line catheter ablation of AF to antiarrhythmic drugs in 294 patients. At 2 years, significantly more patients in the ablation group were free from any AF and symptomatic AF. Quality of life was significantly better in the catheter ablation arm. In Radiofrequency Ablation vs. Antiarrhythmic Drugs as First-Line Treatment of Paroxysmal Atrial Fibrillation (RAAFT-2) trial,[9] the recurrence rate of AF was significant lower after ablation compared with antiarrhythmic drugs after 2 years among 127 patients with paroxysmal AF without previous antiarrhythmic drug treatment. Quality of life improved in both treatment groups. Takigawa et al.[117] have reported long-term follow-up results of catheter ablation of paroxysmal AF in 1220 patients. AF recurrence–free survival probabilities at 5 years were 59.4% after the initial catheter ablation and 81.1% after the final catheter ablation (average, 1.3 procedures). Similar results were found when cryoenergy was used for ablation of AF for treatment-naive patients in Sustained Treatment of Paroxysmal Atrial Fibrillation (STOP- AF) trial.[118] There is only little evidence from prospective, randomized, multicenter clinical trials in patients with chronic AF. However, the recently published prospective randomized Tailored Treatment of Persistent Atrial Fibrillation (TTOP-AF) trial in patients with persistent and long-standing persistent AF demonstrated a significant greater reduction of AF at 6 months after ablation compared with medical treatment.[119] Despite an identical outer shape with the first-generation (Arctic Front; Medtronic Inc, Minneapolis, MN) (Arc- CB), modifications to the refrigerant injection system has allowed improved cooling of the distal balloon hemisphere in the second-generation cryoballoon (Arctic Front Advance; Medtronic Inc, Minneapolis, MN) (Arc- Adv- CB). Several studies have compared the safety and efficacy of cryoablation in patients who underwent ablation with either first or second-generation cryoballoon[120-123] and have shown that Arc-Adv-CB attained high rates of acute PV isolation within a significantly faster and less complex procedure. Recently, Metzner et al.[124] have reported that the use of second-generation 28-mm cryoballoon for PVI resulted in 1-year success rates of 81% for PAF, 77% for short-term persistent AF. Mugnai et al.[125] have reported that at a mean follow-up of 23 months, the success rate was similar for both RFCA and cryoablation groups. Procedural times were significantly shorter in the cryoablation group. Complication rates were similar in both groups except for phrenic nerve palsy that was uniquely observed in the CB group. Wasserlauf et al.[126] have compared 1 year outcomes of cryoballoon and RFCA and shown that cryoballoon ablation was associated with equivalent 1-year freedom from AF rate as RFCA for paroxysmal AF. Procedure and fluoroscopy times were shorter for cryoballoon ablation. Aryana et al.[127] have recently shown that freedom from AF/atrial flutter/tachycardia at 12 months following a single procedure without antiarrhythmic therapy was statistically significantly greater with CB-2 (76.6%) versus RF (60.4%). This difference was evident in patients with paroxysmal AF, it did not reach significance in those with persistent AF.

Currently, there is a lack of evidence and a large debate about the optimal ablation strategy in patients with non-paroxysmal AF. A previous meta-analysis of studies reporting the results of catheter ablation of persistent and long-standing persistent had concluded that the success rate of different strategies is similar, provided that pulmonary vein isolation was performed.[128] A recent systematic review and meta- analysis of randomized and non- randomized controlled trials reporting clinical outcomes after catheter ablation for persistent atrial fibrillation, which included 46 studies containing 3819 patients, has concluded that catheter ablation results in a significantly greater freedom from recurrent AF compared with medical therapy. The most efficacious strategy was reported to be the combination of isolation of the PVs with limited linear ablation within the LA.[129]

It should not be forgotten that although most trials evaluate success of ablation in terms of long-term maintenance of SR, clinical improvement following ablation is often under-evaluated in studies. This clinical improvement may be attributed to a decreased AF burden, alteration in the severity of AF, or changes in overall cardiac function, both in patients with paroxysmal[130,131] or persistent AF.[132] A study has shown that catheter ablation significantly improved quality of life for patients with persistent AF whereas medical therapy had no appreciable effect.[133] There is currently no data on the impact of catheter ablation on mortality. Its impact on mortality (and other secondary outcomes) is being explored in the ongoing Catheter Ablation vs Anti-Arrhythmic Drug Therapy for Atrial Fibrillation (CABANA) trial.

Conclusions

Rhythm control strategy using an invasive catheter ablation therapy is both effective and safe, however, selection of both appropriate patients and ablation technique should be personalized considering various factors like availability of the devices, operators' experience, patient co-morbidities, presence of structural heart disease and patient consent. Thus, we can propose that one strategy does not fit to all AF patients when catheter ablation was chosen as an therapeutic option.

References

1. Chugh Sumeet S, HavmoellerRasmus, NarayananKumar, SinghDavid, RienstraMichiel, BenjaminEmelia J, GillumRichard F, KimYoung-Hoon, McAnultyJohn H, ZhengZhi-Jie, ForouzanfarMohammad H, NaghaviMohsen, MensahGeorge A, EzzatiMajid, MurrayChristopher J L. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation. 2014;129 (8):837–47.
2. Haïssaguerre M, JaïsP, ShahD C, TakahashiA, HociniM, QuiniouG, GarrigueS, Le MourouxA, Le MétayerP, ClémentyJ. Spontaneous initiation of atrial

fibrillation by ectopic beats originating in the pulmonary veins. N. Engl. J. Med. 1998;339 (10):659–66.

3. Calkins Hugh, KuckKarl Heinz, CappatoRiccardo, BrugadaJosep, CammA John, ChenShih-Ann, CrijnsHarry J G, DamianoRalph J, DaviesD Wyn, DiMarcoJohn, EdgertonJames, EllenbogenKenneth, EzekowitzMichael D, HainesDavid E, HaissaguerreMichel, HindricksGerhard, IesakaYoshito, JackmanWarren, JalifeJosé, JaisPierre, KalmanJonathan, KeaneDavid, KimYoung-Hoon, KirchhofPaulus, KleinGeorge, KottkampHans, KumagaiKoichiro, LindsayBruce D, MansourMoussa, MarchlinskiFrancis E, McCarthyPatrick M, MontJ Lluis, MoradyFred, NademaneeKoonlawee, NakagawaHiroshi, NataleAndrea, NattelStanley, PackerDouglas L, PapponeCarlo, PrystowskyEric, RavieleAntonio, ReddyVivek, RuskinJeremy N, SheminRichard J, TsaoHsuan-Ming, WilberDavid. 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. 2012;9 (4):632–696.e21.
4. Terasawa Teruhiko, BalkEthan M, ChungMei, GarlitskiAnn C, Alsheikh-AliAlawi A, LauJoseph, IpStanley. Systematic review: comparative effectiveness of radiofrequency catheter ablation for atrial fibrillation. Ann. Intern. Med. 2009;151 (3):191–202.
5. Nair Girish M, NeryPablo B, DiwakaramenonSyamkumar, HealeyJeffrey S, ConnollyStuart J, MorilloCarlos A. A systematic review of randomized trials comparing radiofrequency ablation with antiarrhythmic medications in patients with atrial fibrillation. J. Cardiovasc. Electrophysiol. 2009;20 (2):138–44.
6. Calkins Hugh, ReynoldsMatthew R, SpectorPeter, SondhiManu, XuYingxin, MartinAmber, WilliamsCatherine J, SledgeIsabella. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. Circ Arrhythm Electrophysiol. 2009;2 (4):349–61.
7. Wazni Oussama M, MarroucheNassir F, MartinDavid O, VermaAtul, BhargavaMandeep, SalibaWalid, BashDianna, SchweikertRobert, BrachmannJohannes, GuntherJens, GutlebenKlaus, PisanoEnnio, PotenzaDominico, FanelliRaffaele, RavieleAntonio, ThemistoclakisSakis, RossilloAntonio, BonsoAldo, NataleAndrea. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. JAMA. 2005;293 (21):2634–40.
8. Raatikainen M J Pekka, HakalahtiAntti, UusimaaPaavo, NielsenJens Cosedis, JohannessenArne, HindricksGerhard, WalfridssonHåkan, PehrsonSteen, EnglundAnders, HartikainenJuha, KongstadOle, MortensenLeif Spange, HansenPeter Steen. Radiofrequency catheter ablation maintains its efficacy better than antiarrhythmic medication in patients with paroxysmal atrial fibrillation: On-treatment analysis of the randomized controlled MANTRA-PAF trial. Int. J. Cardiol. 2015;198:108–14.
9. Morillo Carlos A, VermaAtul, ConnollyStuart J, KuckKarl H, NairGirish M, ChampagneJean, SternsLaurence D, BereshHeather, HealeyJeffrey S, NataleAndrea. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation (RAAFT-2): a randomized trial. JAMA. 2014;311 (7):692–700.
10. Wokhlu Anita, MonahanKristi H, HodgeDavid O, AsirvathamSamuel J, FriedmanPaul A, MungerThomas M, BradleyDavid J, BluhmChristine M, HaroldsonJanis M, PackerDouglas L. Long-term quality of life after ablation of atrial fibrillation the impact of recurrence, symptom relief, and placebo effect. J. Am. Coll. Cardiol. 2010;55 (21):2308–16.
11. January Craig T, WannL Samuel, AlpertJoseph S, CalkinsHugh, CigarroaJoaquin E, ClevelandJoseph C, ContiJamie B, EllinorPatrick T, EzekowitzMichael D, FieldMichael E, MurrayKatherine T, SaccoRalph L, StevensonWilliam G, TchouPatrick J, TracyCynthia M, YancyClyde W. 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. 2014;64 (21):e1–76.
12. Camm A John, LipGregory Y H, De CaterinaRaffaele, SavelievaIrene, AtarDan, HohnloserStefan H, HindricksGerhard, KirchhofPaulus. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation--developed with the special contribution of the European Heart Rhythm Association. Europace. 2012;14 (10):1385–413.
13. Pathak Rajeev K, MiddeldorpMelissa E, LauDennis H, MehtaAbhinav B, MahajanRajiv, TwomeyDarragh, AlasadyMuayad, HanleyLorraine, AnticNicholas A, McEvoyR Doug, KalmanJonathan M, AbhayaratnaWalter P, SandersPrashanthan. Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation: the ARREST-AF cohort study. J. Am. Coll. Cardiol. 2014;64 (21):2222–31.
14. Hsu Li-Fern, JaïsPierre, SandersPrashanthan, GarrigueStéphane, HociniMélèze, SacherFréderic, TakahashiYoshihide, RotterMartin, PasquiéJean-Luc, ScavéeChristophe, BordacharPierre, ClémentyJacques, HaïssaguerreMichel. Catheter ablation for atrial fibrillation in congestive heart failure. N. Engl. J. Med. 2004;351 (23):2373–83.
15. Khan Mohammed N, JaïsPierre, CummingsJennifer, Di BiaseLuigi, SandersPrashanthan, MartinDavid O, KautznerJosef, HaoSteven, ThemistoclakisSakis, FanelliRaffaele, PotenzaDomenico, MassaroRaimondo, WazniOussama, SchweikertRobert, SalibaWalid, WangPaul, Al-AhmadAmin, BeheirySalwa, SantarelliPietro, StarlingRandall C, Dello RussoAntonio, PelargonioGemma, BrachmannJohannes, SchibgillaVolker, BonsoAldo, CasellaMichela, RavieleAntonio, HaïssaguerreMichel, NataleAndrea. Pulmonary-vein isolation for atrial fibrillation in patients with heart failure. N. Engl. J. Med. 2008;359 (17):1778–85.
16. Jones David G, HaldarShouvik K, HussainWajid, SharmaRakesh, FrancisDarrel P, Rahman-HaleyShelley L, McDonaghTheresa A, UnderwoodS Richard, MarkidesVias, WongTom. A randomized trial to assess catheter ablation versus rate control in the management of persistent atrial fibrillation in heart failure. J. Am. Coll. Cardiol. 2013;61 (18):1894–903.
17. Dagres Nikolaos, VarounisChristos, GasparThomas, PiorkowskiChristopher, EitelCharlotte, IliodromitisEfstathios K, LekakisJohn P, FlevariPanayota, SimeonidouEftihia, RallidisLoukianos S, TsougosElias, HindricksGerhard, SommerPhilipp, Anastasiou-NanaMaria. Catheter ablation for atrial fibrillation in patients with left ventricular systolic dysfunction. A systematic review and meta-analysis. J. Card. Fail. 2011;17 (11):964–70.
18. Roy Denis, TalajicMario, NattelStanley, WyseD George, DorianPaul, LeeKerry L, BourassaMartial G, ArnoldJ Malcolm O, BuxtonAlfred E, CammA John, ConnollyStuart J, DubucMarc, DucharmeAnique, GuerraPeter G, HohnloserStefan H, LambertJean, Le HeuzeyJean-Yves, O'HaraGilles, PedersenOle Dyg, RouleauJean-Lucien, SinghBramah N, StevensonLynne Warner, StevensonWilliam G, ThibaultBernard, WaldoAlbert L. Rhythm control versus rate control for atrial fibrillation and heart failure. N. Engl. J. Med. 2008;358 (25):2667–77.

19. Cha Yong-Mei, WokhluAnita, AsirvathamSamuel J, ShenWin-Kuang, FriedmanPaul A, MungerThomas M, OhJae K, MonahanKristi H, HaroldsonJanis M, HodgeDavid O, HergesRegina M, HammillStephen C, PackerDouglas L. Success of ablation for atrial fibrillation in isolated left ventricular diastolic dysfunction: a comparison to systolic dysfunction and normal ventricular function. Circ Arrhythm Electrophysiol. 2011;4 (5):724–32.
20. Wilton Stephen B, FundytusAdam, GhaliWilliam A, VeenhuyzenGeorge D, QuinnF Russell, MitchellL Brent, HillMichael D, FarisPeter, ExnerDerek V. Meta-analysis of the effectiveness and safety of catheter ablation of atrial fibrillation in patients with versus without left ventricular systolic dysfunction. Am. J. Cardiol. 2010;106 (9):1284–91.
21. Rillig Andreas, MakimotoHisaki, WegnerJascha, LinTina, HeegerChristian, LemesChristine, FinkThomas, MetznerAndreas, WissnerErik, MathewShibu, WohlmuthPeter, KuckKarl-Heinz, TilzRoland Richard, OuyangFeifan. Six-Year Clinical Outcomes After Catheter Ablation of Atrial Fibrillation in Patients With Impaired Left Ventricular Function. J. Cardiovasc. Electrophysiol. 2015;.
22. Bunch T Jared, MayHeidi T, BairTami L, JacobsVictoria, CrandallBrian G, CutlerMichael, WeissJ Peter, MallenderCharles, OsbornJeffrey S, AndersonJeffrey L, DayJohn D. Five-year outcomes of catheter ablation in patients with atrial fibrillation and left ventricular systolic dysfunction. J. Cardiovasc. Electrophysiol. 2015;26 (4):363–70.
23. Anselmino Matteo, MattaMario, D'AscenzoFabrizio, BunchT Jared, SchillingRichard J, HunterRoss J, PapponeCarlo, NeumannThomas, NoelkerGeorg, FialaMartin, BertagliaEmanuele, FronteraAntonio, DuncanEdward, NalliahChrishan, JaisPierre, WeerasooriyaRukshen, KalmanJon M, GaitaFiorenzo. Catheter ablation of atrial fibrillation in patients with left ventricular systolic dysfunction: a systematic review and meta-analysis. Circ Arrhythm Electrophysiol. 2014;7 (6):1011–8.
24. Al Halabi Shadi, QintarMohammed, HusseinAyman, AlraiesM Chadi, JonesDavid G, WongTom, MacDonaldMichael R, PetrieMark C, CantillonDaniel, TarakjiKhaldoun G, KanjMohamed, BhargavaMandeep, VarmaNiraj, BaranowskiBryan, WilkoffBruce L, WazniOussama, CallahanThomas, SalibaWalid, ChungMina K. Catheter Ablation for Atrial Fibrillation in Heart Failure Patients: A Meta-Analysis of Randomized Controlled Trials. JACC Clin Electrophysiol. 2015;1 (3):200–209.
25. Kumar Prabhat, PatelAnkit, MounseyJ Paul, ChungEugene H, SchwartzJennifer D, PursellIrion W, GehiAnil K. Effect of left ventricular diastolic dysfunction on outcomes of atrial fibrillation ablation. Am. J. Cardiol. 2014;114 (3):407–11.
26. Tuan Ta-Chuan, ChangShih-Lin, TsaoHsuan-Ming, TaiChing-Tai, LinYenn-Jiang, HuYu-Feng, LoLi-Wei, UdyavarAmeya R, ChangChien-Jong, TsaiWen-Chin, TangWei-Hua, SuenariKazuyoshi, HuangShih-Yu, LeePi-Change, ChenShih-Ann. The impact of age on the electroanatomical characteristics and outcome of catheter ablation in patients with atrial fibrillation. J. Cardiovasc. Electrophysiol. 2010;21 (9):966–72.
27. Hsieh Ming-Hsiung, TaiChing-Tai, LeeShih-Huang, TsaoHuan-Ming, LinYung-Kuo, HuangJin-Long, ChanPaul, ChenYi-Jen, KuoJen-Yuan, TuanTa-Chuan, HsuTsui-Lieh, KongChi-Woon, ChangShih-Lin, ChenShih-Ann. Catheter ablation of atrial fibrillation versus atrioventricular junction ablation plus pacing therapy for elderly patients with medically refractory paroxysmal atrial fibrillation. J. Cardiovasc. Electrophysiol. 2005;16 (5):457–61.
28. Corrado Andrea, PatelDimpi, RiedlbauchovaLucie, FahmyTamer S, ThemistoclakisSakis, BonsoAldo, RossilloAntonio, HaoSteven, SchweikertRobert A, CummingsJennifer E, BhargavaMandeep, BurkhardtDavid, SalibaWalid, RavieleAntonio, NataleAndrea. Efficacy, safety, and outcome of atrial fibrillation ablation in septuagenarians. J. Cardiovasc. Electrophysiol. 2008;19 (8):807–11.
29. Zado Erica, CallansDavid J, RileyMichael, HutchinsonMathew, GarciaFermin, BalaRupa, LinDavid, CooperJoshua, VerdinoRalph, RussoAndrea M, DixitSanjay, GerstenfeldEdward, MarchlinskiFrancis E. Long-term clinical efficacy and risk of catheter ablation for atrial fibrillation in the elderly. J. Cardiovasc. Electrophysiol. 2008;19 (6):621–6.
30. Leong-Sit Peter, ZadoErica, CallansDavid J, GarciaFermin, LinDavid, DixitSanjay, BalaRupa, RileyMichael P, HutchinsonMathew D, CooperJoshua, GerstenfeldEdward P, MarchlinskiFrancis E. Efficacy and risk of atrial fibrillation ablation before 45 years of age. Circ Arrhythm Electrophysiol. 2010;3 (5):452–7.
31. Bunch T Jared, WeissJ Peter, CrandallBrian G, MayHeidi T, BairTami L, OsbornJeffrey S, AndersonJeffrey L, LappeDonald L, MuhlesteinJ Brent, NelsonJennifer, DayJohn D. Long-term clinical efficacy and risk of catheter ablation for atrial fibrillation in octogenarians. Pacing Clin Electrophysiol. 2010;33 (2):146–52.
32. Santangeli Pasquale, Di BiaseLuigi, MohantyPrasant, BurkhardtJ David, HortonRodney, BaiRong, MohantySanghamitra, PumpAgnes, GibsonDouglas, CoutsLinda, HongoRichard, BeheirySalwa, NataleAndrea. Catheter ablation of atrial fibrillation in octogenarians: safety and outcomes. J. Cardiovasc. Electrophysiol. 2012;23 (7):687–93.
33. Spragg David D, DalalDarshan, CheemaAamir, ScherrDaniel, ChilukuriKaruna, ChengAlan, HenriksonCharles A, MarineJoseph E, BergerRonald D, DongJun, CalkinsHugh. Complications of catheter ablation for atrial fibrillation: incidence and predictors. J. Cardiovasc. Electrophysiol. 2008;19 (6):627–31.
34. Shah Rashmee U, FreemanJames V, ShilaneDavid, WangPaul J, GoAlan S, HlatkyMark A. Procedural complications, rehospitalizations, and repeat procedures after catheter ablation for atrial fibrillation. J. Am. Coll. Cardiol. 2012;59 (2):143–9.
35. Contreras-Valdes Fernando M, BuxtonAlfred E, JosephsonMark E, AnterElad. Atrial fibrillation ablation in patients with hypertrophic cardiomyopathy: long-term outcomes and clinical predictors. J. Am. Coll. Cardiol. 2015;65 (14):1485–7.
36. Gaita Fiorenzo, Di DonnaPaolo, OlivottoIacopo, ScaglioneMarco, FerreroIvana, MontefuscoAntonio, CaponiDomenico, ConteMaria Rosa, NistriStefano, CecchiFranco. Usefulness and safety of transcatheter ablation of atrial fibrillation in patients with hypertrophic cardiomyopathy. Am. J. Cardiol. 2007;99 (11):1575–81.
37. Bunch T Jared, MungerThomas M, FriedmanPaul A, AsirvathamSamuel J, BradyPeter A, ChaYong-Mei, ReaRobert F, ShenWin-Kuang, PowellBrian D, OmmenSteve R, MonahanKristi H, HaroldsonJanis M, PackerDouglas L. Substrate and procedural predictors of outcomes after catheter ablation for atrial fibrillation in patients with hypertrophic cardiomyopathy. J. Cardiovasc. Electrophysiol. 2008;19 (10):1009–14.
38. Okamatsu Hideharu, OharaTakahiro, KanzakiHideaki, NakajimaIkutaro, MiyamotoKoji, OkamuraHideo, NodaTakashi, AibaTakeshi, KusanoKengo, KamakuraShiro, ShimizuWataru, SatomiKazuhiro. Impact of left ventricular diastolic dysfunction on outcome of catheter ablation for atrial fibrillation in patients with hypertrophic cardiomyopathy. Circ. J. 2015;79 (2):419–24.
39. Bassiouny Mohamed, LindsayBruce D, LeverHarry, SalibaWalid, KleinAllan, BannaMoustafa, AbrahamJoEllyn, ShaoMingyuan, RickardJohn, KanjMohamed, TchouPatrick, DresingThomas, BaranowskiBryan, BhargavaMandeep, CallahanThomas, TarakjiKhaldoun, CantillonDaniel, HusseinAyman, Marc GillinovA, SmediraNicholas G, WazniOussama. Outcomes of nonpharmacologic treatment of atrial fibrillation in patients with hypertrophic cardiomyopathy. Heart Rhythm. 2015;12 (7):1438–47.
40. Bortone Agustín, AppetitiAnthony. Successful radiofrequency ablation of persistent atrial fibrillation in a patient with mechanical mitral valve prosthesis: utility of merging computed tomography of the left atrium with its electroanatomic mapping reconstruction. Heart Rhythm. 2009;6 (9):1388–9.
41. Lang Christopher C, SantinelliVincenzo, AugelloGiuseppe, FerroAmedeo, GugliottaFilippo, GullettaSimone, VicedominiGabriele, MesasCézar, PaglinoGabriele, SalaSimone, SoraNicoleta, MazzonePatrizio, MangusoFrancesco, PapponeCarlo. Transcatheter radiofrequency ablation of atrial fibrillation in

patients with mitral valve prostheses and enlarged atria: safety, feasibility, and efficacy. J. Am. Coll. Cardiol. 2005;45 (6):868–72.

42. Lakkireddy Dhanunjaya, NagarajanDarbhamulla, Di BiaseLuigi, VangaSubba Reddy, MahapatraSrijoy, Jared BunchT, DayJohn D, BurkhardtDavid J, UmbargerLinda, DendiRaghuveer, PimentelRhea, BerenbomLoren, EmertMartin, GerkenAnna, BommanaSudharani, RayWallace, AtkinsDonita, MurrayCaroline, DawnBuddhadeb, NataleAndrea. Radiofrequency ablation of atrial fibrillation in patients with mitral or aortic mechanical prosthetic valves: a feasibility, safety, and efficacy study. Heart Rhythm. 2011;8 (7):975–80.
43. Hussein Ayman A, WazniOussama M, HarbSerge, JosephLee, Chamsi-PashaMohammed, BhargavaMandeep, MartinDavid O, DresingThomas, CallahanThomas, KanjMohamed, NataleAndrea, LindsayBruce D, SalibaWalid I. Radiofrequency ablation of atrial fibrillation in patients with mechanical mitral valve prostheses safety, feasibility, electrophysiologic findings, and outcomes. J. Am. Coll. Cardiol. 2011;58 (6):596–602.
44. Bai Rong, di BiaseLuigi, MohantyPrasant, SantangeliPasquale, MohantySanghamitra, PumpAgnes, ElayiClaude S, ReddyYeruva Madhu, ForleoGiovanni B, HongoRichard, BeheirySalwa, Dello RussoAntonio, CasellaMichela, PelargonioGemma, SantarelliPietro, HortonRodney, SanchezJavier, GallinghouseJoseph, BurkhardtJ David, MaChangsheng, LakkireddyDhanunjaya, TondoClaudio, NataleAndrea. Catheter ablation of atrial fibrillation in patients with mechanical mitral valve: long-term outcome of single procedure of pulmonary vein antrum isolation with or without nonpulmonary vein trigger ablation. J. Cardiovasc. Electrophysiol. 2014;25 (8):824–33.
45. Calvo Naiara, MontLluís, TamboreroDavid, BerruezoAntonio, ViolaGraziana, GuaschEduard, NadalMercè, AndreuDavid, VidalBarbara, SitgesMarta, BrugadaJosep. Efficacy of circumferential pulmonary vein ablation of atrial fibrillation in endurance athletes. Europace. 2010;12 (1):30–6.
46. Khairy Paul, GuerraPeter G, RivardLena, TanguayJean-François, LandryEvelyn, GuertinMarie-Claude, MacleLaurent, ThibaultBernard, TardifJean-Claude, TalajicMario, RoyDenis, DubucMarc. Enlargement of catheter ablation lesions in infant hearts with cryothermal versus radiofrequency energy: an animal study. Circ Arrhythm Electrophysiol. 2011;4 (2):211–7.
47. Kobza Richard, HindricksGerhard, TannerHildegard, SchirdewahnPetra, DorszewskiAnja, PiorkowskiChristopher, Gerds-LiJin-Hong, KottkampHans. Late recurrent arrhythmias after ablation of atrial fibrillation: incidence, mechanisms, and treatment. Heart Rhythm. 2004;1 (6):676–83.
48. Akoum Nazem, DaccarettMarcos, McGannChris, SegersonNathan, VergaraGaston, KuppahallySuman, BadgerTroy, BurgonNathan, HaslamThomas, KholmovskiEugene, MacleodRob, MarroucheNassir. Atrial fibrosis helps select the appropriate patient and strategy in catheter ablation of atrial fibrillation: a DE-MRI guided approach. J. Cardiovasc. Electrophysiol. 2011;22 (1):16–22.
49. Oakes Robert S, BadgerTroy J, KholmovskiEugene G, AkoumNazem, BurgonNathan S, FishEric N, BlauerJoshua J E, RaoSwati N, DiBellaEdward V R, SegersonNathan M, DaccarettMarcos, WindfelderJessiciah, McGannChristopher J, ParkerDennis, MacLeodRob S, MarroucheNassir F. Detection and quantification of left atrial structural remodeling with delayed-enhancement magnetic resonance imaging in patients with atrial fibrillation. Circulation. 2009;119 (13):1758–67.
50. Marrouche Nassir F, WilberDavid, HindricksGerhard, JaisPierre, AkoumNazem, MarchlinskiFrancis, KholmovskiEugene, BurgonNathan, HuNan, MontLluis, DenekeThomas, DuytschaeverMattias, NeumannThomas, MansourMoussa, MahnkopfChristian, HerwegBengt, DaoudEmile, WissnerErik, BansmannPaul, BrachmannJohannes. Association of atrial tissue fibrosis identified by delayed enhancement MRI and atrial fibrillation catheter ablation: the DECAAF study. JAMA. 2014;311 (5):498–506.
51. Gurses Kadri Murat, YalcinMuhammed Ulvi, KocyigitDuygu, KesikliSacit Altug, CanpolatUgur, YorgunHikmet, SahinerMehmet Levent, KayaErgun Baris, HazirolanTuncay, OzerNecla, OtoMehmet Ali, GucDicle, AytemirKudret. M2-muscarinic acetylcholine receptor autoantibody levels predict left atrial fibrosis severity in paroxysmal lone atrial fibrillation patients undergoing cryoablation. Europace. 2015;17 (2):239–46.
52. Ranjan Ravi, KholmovskiEugene G, BlauerJoshua, VijayakumarSathya, VollandNelly A, SalamaMohamed E, ParkerDennis L, MacLeodRob, MarroucheNassir F. Identification and acute targeting of gaps in atrial ablation lesion sets using a real-time magnetic resonance imaging system. Circ Arrhythm Electrophysiol. 2012;5 (6):1130–5.
53. Nazarian Saman, KolandaiveluAravindan, ZvimanMenekhem M, MeiningerGlenn R, KatoRitsushi, SusilRobert C, RoguinAriel, DickfeldTimm L, AshikagaHiroshi, CalkinsHugh, BergerRonald D, BluemkeDavid A, LardoAlbert C, HalperinHenry R. Feasibility of real-time magnetic resonance imaging for catheter guidance in electrophysiology studies. Circulation. 2008;118 (3):223–9.
54. Macle Laurent, KhairyPaul, WeerasooriyaRukshen, NovakPaul, VermaAtul, WillemsStephan, ArentzThomas, DeisenhoferIsabel, VeenhuyzenGeorge, ScavéeChristophe, JaïsPierre, PuererfellnerHelmut, LevesqueSylvie, AndradeJason G, RivardLena, GuerraPeter G, DubucMarc, ThibaultBernard, TalajicMario, RoyDenis, NattelStanley. Adenosine-guided pulmonary vein isolation for the treatment of paroxysmal atrial fibrillation: an international, multicentre, randomised superiority trial. Lancet. 2015;386 (9994):672–9.
55. Kobori Atsushi, ShizutaSatoshi, InoueKoichi, KaitaniKazuaki, MorimotoTakeshi, NakazawaYuko, OzawaTomoya, KurotobiToshiya, MorishimaItsuro, MiuraFumiharu, WatanabeTetsuya, MasudaMasaharu, NaitoMasaki, FujimotoHajime, NishidaTaku, FurukawaYoshio, ShirayamaTakeshi, TanakaMariko, OkajimaKatsunori, YaoTakenori, EgamiYasuyuki, SatomiKazuhiro, NodaTakashi, MiyamotoKoji, HarunaTetsuya, KawajiTetsuma, YoshizawaTakashi, ToyotaToshiaki, YahataMitsuhiko, NakaiKentaro, SugiyamaHiroaki, HigashiYukei, ItoMakoto, HorieMinoru, KusanoKengo F, ShimizuWataru, KamakuraShiro, KimuraTakeshi. Adenosine triphosphate-guided pulmonary vein isolation for atrial fibrillation: the UNmasking Dormant Electrical Reconduction by Adenosine TriPhosphate (UNDER-ATP) trial. Eur. Heart J. 2015;36 (46):3276–87.
56. Hocini Mélèze, JaïsPierre, SandersPrashanthan, TakahashiYoshihide, RotterMartin, RostockThomas, HsuLi-Fern, SacherFrédéric, ReuterSylvain, ClémentyJacques, HaïssaguerreMichel. Techniques, evaluation, and consequences of linear block at the left atrial roof in paroxysmal atrial fibrillation: a prospective randomized study. Circulation. 2005;112 (24):3688–96.
57. Verma Atul, JiangChen-yang, BettsTimothy R, ChenJian, DeisenhoferIsabel, MantovanRoberto, MacleLaurent, MorilloCarlos A, HaverkampWilhelm, WeerasooriyaRukshen, AlbenqueJean-Paul, NardiStefano, MenardiEndrj, NovakPaul, SandersPrashanthan. Approaches to catheter ablation for persistent atrial fibrillation. N. Engl. J. Med. 2015;372 (19):1812–22.
58. Haïssaguerre M, JaïsP, ShahD C, GarrigueS, TakahashiA, LavergneT, HociniM, PengJ T, RoudautR, ClémentyJ. Electrophysiological end point for catheter ablation of atrial fibrillation initiated from multiple pulmonary venous foci. Circulation. 2000;101 (12):1409–17.
59. Pappone C, RosanioS, OretoG, TocchiM, GugliottaF, VicedominiG, SalvatiA, DicandiaC, MazzoneP, SantinelliV, GullettaS, ChierchiaS. Circumferential radiofrequency ablation of pulmonary vein ostia: A new anatomic approach for curing atrial fibrillation. Circulation. 2000;102 (21):2619–28.
60. Ernst Sabine, OuyangFeifan, LöberFelix, AntzMatthias, KuckKarl-Heinz. Catheter-induced linear lesions in the left atrium in patients with atrial fibrillation: an electroanatomic study. J. Am. Coll. Cardiol. 2003;42 (7):1271–82.
61. Sawhney Navinder, AnoushehRamtin, ChenWei, FeldGregory K. Circumferential pulmonary vein ablation with additional linear ablation results in an increased incidence of left atrial flutter compared with segmental pulmonary vein isolation as an initial approach to ablation of paroxysmal atrial fibrillation. Circ Arrhythm Electrophysiol. 2010;3 (3):243–8.

62. Verma Atul. The techniques for catheter ablation of paroxysmal and persistent atrial fibrillation: a systematic review. Curr. Opin. Cardiol. 2011;26 (1):17–24.
63. Gaita Fiorenzo, CaponiDomenico, ScaglioneMarco, MontefuscoAntonio, CorletoAntonella, Di MonteFernando, CoinDaniele, Di DonnaPaolo, GiustettoCarla. Long-term clinical results of 2 different ablation strategies in patients with paroxysmal and persistent atrial fibrillation. Circ Arrhythm Electrophysiol. 2008;1 (4):269–75.
64. Lee Shih-Huang, TaiChing-Tai, HsiehMing-Hsiung, TsaoHsuan-Ming, LinYenn-Jiang, ChangShih-Lin, HuangJin-Long, LeeKun-Tai, ChenYi-Jen, ChengJun-Jack, ChenShih-Ann. Predictors of non-pulmonary vein ectopic beats initiating paroxysmal atrial fibrillation: implication for catheter ablation. J. Am. Coll. Cardiol. 2005;46 (6):1054–9.
65. Lin Wei-Shiang, TaiChing-Tai, HsiehMing-Hsiung, TsaiChin-Feng, LinYung-Kuo, TsaoHsuan-Ming, HuangJin-Long, YuWen-Chung, YangShih-Ping, DingYu-An, ChangMau-Song, ChenShih-Ann. Catheter ablation of paroxysmal atrial fibrillation initiated by non-pulmonary vein ectopy. Circulation. 2003;107 (25):3176–83.
66. Chen Shih-Ann, TaiChing-Tai. Catheter ablation of atrial fibrillation originating from the non-pulmonary vein foci. J. Cardiovasc. Electrophysiol. 2005;16 (2):229–32.
67. Verma Atul, MantovanRoberto, MacleLaurent, De MartinoGuiseppe, ChenJian, MorilloCarlos A, NovakPaul, CalzolariVittorio, GuerraPeter G, NairGirish, TorrecillaEsteban G, KhaykinYaariv. Substrate and Trigger Ablation for Reduction of Atrial Fibrillation (STAR AF): a randomized, multicentre, international trial. Eur. Heart J. 2010;31 (11):1344–56.
68. Estner Heidi Luise, HesslingGabriele, NdrepepaGjin, WuJinjin, ReentsTilko, FichtnerStefanie, SchmittClaus, BaryChristian V, KolbChristof, KarchMartin, ZrennerBernhard, DeisenhoferIsabel. Electrogram-guided substrate ablation with or without pulmonary vein isolation in patients with persistent atrial fibrillation. Europace. 2008;10 (11):1281–7.
69. Deisenhofer Isabel, EstnerHeidi, ReentsTilko, FichtnerStephanie, BauerAxel, WuJinjin, KolbChristof, ZrennerBernhard, SchmittClaus, HesslingGabriele. Does electrogram guided substrate ablation add to the success of pulmonary vein isolation in patients with paroxysmal atrial fibrillation? A prospective, randomized study. J. Cardiovasc. Electrophysiol. 2009;20 (5):514–21.
70. Di Biase Luigi, ElayiClaude S, FahmyTamer S, MartinDavid O, ChingChi Keong, BarrettConor, BaiRong, PatelDimpi, KhaykinYaariv, HongoRichard, HaoSteven, BeheirySalwa, PelargonioGemma, Dello RussoAntonio, CasellaMichela, SantarelliPietro, PotenzaDomenico, FanelliRaffaele, MassaroRaimondo, WangPaul, Al-AhmadAmin, ArrudaMauricio, ThemistoclakisSakis, BonsoAldo, RossilloAntonio, RavieleAntonio, SchweikertRobert A, BurkhardtDavid J, NataleAndrea. Atrial fibrillation ablation strategies for paroxysmal patients: randomized comparison between different techniques. Circ Arrhythm Electrophysiol. 2009;2 (2):113–9.
71. Elayi Claude S, VermaAtul, Di BiaseLuigi, ChingChi Keong, PatelDimpi, BarrettConor, MartinDavid, RongBai, FahmyTamer S, KhaykinYaariv, HongoRichard, HaoSteven, PelargonioGemma, Dello RussoAntonio, CasellaMichela, SantarelliPietro, PotenzaDomenico, FanelliRaffaele, MassaroRaimondo, ArrudaMauricio, SchweikertRobert A, NataleAndrea. Ablation for longstanding permanent atrial fibrillation: results from a randomized study comparing three different strategies. Heart Rhythm. 2008;5 (12):1658–64.
72. Oral Hakan, ChughAman, YoshidaKentaro, SarrazinJean F, KuhneMichael, CrawfordThomas, ChalfounNagib, WellsDarryl, BoonyapisitWarangkna, VeerareddySrikar, BillakantySreedhar, WongWai S, GoodEric, JongnarangsinKrit, PelosiFrank, BogunFrank, MoradyFred. A randomized assessment of the incremental role of ablation of complex fractionated atrial electrograms after antral pulmonary vein isolation for long-lasting persistent atrial fibrillation. J. Am. Coll. Cardiol. 2009;53 (9):782–9.
73. Pokushalov Evgeny, RomanovAlexander, ArtyomenkoSergey, TurovAlex, ShirokovaNatalya, KatritsisDemosthenes G. Left atrial ablation at the anatomic areas of ganglionated plexi for paroxysmal atrial fibrillation. Pacing Clin Electrophysiol. 2010;33 (10):1231–8.
74. Katritsis Demosthenes G, GiazitzoglouEleftherios, ZografosTheodoros, PokushalovEvgeny, PoSunny S, CammA John. Rapid pulmonary vein isolation combined with autonomic ganglia modification: a randomized study. Heart Rhythm. 2011;8 (5):672–8.
75. Narayan Sanjiv M, BaykanerTina, CloptonPaul, SchrickerAmir, LalaniGautam G, KrummenDavid E, ShivkumarKalyanam, MillerJohn M. Ablation of rotor and focal sources reduces late recurrence of atrial fibrillation compared with trigger ablation alone: extended follow-up of the CONFIRM trial (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation). J. Am. Coll. Cardiol. 2014;63 (17):1761–8.
76. Narayan Sanjiv M, KrummenDavid E, CloptonPaul, ShivkumarKalyanam, MillerJohn M. Direct or coincidental elimination of stable rotors or focal sources may explain successful atrial fibrillation ablation: on-treatment analysis of the CONFIRM trial (Conventional ablation for AF with or without focal impulse and rotor modulation). J. Am. Coll. Cardiol. 2013;62 (2):138–47.
77. Miyazaki Shinsuke, KuwaharaTaishi, KoboriAtsushi, TakahashiYoshihide, TakeiAsumi, SatoAkira, IsobeMitsuaki, TakahashiAtsushi. Impact of adenosine-provoked acute dormant pulmonary vein conduction on recurrence of atrial fibrillation. J. Cardiovasc. Electrophysiol. 2012;23 (3):256–60.
78. Matsuo Seiichiro, YamaneTeiichi, DateTaro, InadaKeiichi, KanzakiYasuko, TokudaMichifumi, ShibayamaKenri, MiyanagaSatoru, MiyazakiHidekazu, SugimotoKenichi, MochizukiSeibu. Reduction of AF recurrence after pulmonary vein isolation by eliminating ATP-induced transient venous re-conduction. J. Cardiovasc. Electrophysiol. 2007;18 (7):704–8.
79. Matsuo Seiichiro, YamaneTeiichi, DateTaro, LelloucheNicolas, TokutakeKen-Ichi, HiokiMika, ItoKeiichi, NaruiRyohsuke, TanigawaShin-Ichi, NakaneTokiko, TokudaMichifumi, YamashitaSeigo, AramakiYasuko, InadaKeiichi, ShibayamaKenri, MiyanagaSatoru, YoshidaHiroshi, MiyazakiHidekazu, AbeKunihiko, SugimotoKen-Ichi, TaniguchiIkuo, YoshimuraMichihiro. Dormant pulmonary vein conduction induced by adenosine in patients with atrial fibrillation who underwent catheter ablation. Am. Heart J. 2011;161 (1):188–96.
80. Gula Lorne J, MasselDavid, Leong-SitPeter, GrayChristopher, FoxDavid J, SegalOliver R, KrahnAndrew D, YeeRaymond, KleinGeorge J, SkanesAllan C. Does adenosine response predict clinical recurrence of atrial fibrillation after pulmonary vein isolation?. J. Cardiovasc. Electrophysiol. 2011;22 (9):982–6.
81. Kumar Narendra, DinhTrang, PhanKevin, TimmermansCarl, PhilippensSuzanne, DassenWillem, VrankenNousjka, PisonLaurent, MaessenJos, CrijnsHarry J. Adenosine testing after second-generation cryoballoon ablation (ATSCA) study improves clinical success rate for atrial fibrillation. Europace. 2015;17 (6):871–6.
82. Macle Laurent, KhairyPaul, WeerasooriyaRukshen, NovakPaul, VermaAtul, WillemsStephan, ArentzThomas, DeisenhoferIsabel, VeenhuyzenGeorge, ScavéeChristophe, JaïsPierre, PuererfellnerHelmut, LevesqueSylvie, AndradeJason G, RivardLena, GuerraPeter G, DubucMarc, ThibaultBernard, TalajicMario, RoyDenis, NattelStanley. Adenosine-guided pulmonary vein isolation for the treatment of paroxysmal atrial fibrillation: an international, multicentre, randomised superiority trial. Lancet. 2015;386 (9994):672–9.
83. Eitel Charlotte, HindricksGerhard, SommerPhilipp, GasparThomas, KircherSimon, WetzelUlrike, DagresNicos, EsatoMasahiro, BollmannAndreas, HusserDaniela, HilbertSebastian, Zaker-ShahrakRuzbeh, AryaArash, PiorkowskiChristopher. Circumferential pulmonary vein isolation and linear left atrial ablation as a single-catheter technique to achieve bidirectional conduction block: the pace-and-ablate approach. Heart Rhythm. 2010;7 (2):157–64.
84. Steven Daniel, ReddyVivek Y, InadaKeiichi, Roberts-ThomsonKurt C, SeilerJens, StevensonWilliam G, MichaudGregory F. Loss of pace capture on the ablation

line: a new marker for complete radiofrequency lesions to achieve pulmonary vein isolation. Heart Rhythm. 2010;7 (3):323–30.

85. Yamane Teiichi, MatsuoSeiichiro, DateTaro, LelloucheNicolas, HiokiMika, NaruiRyosuke, ItoKeiichi, TanigawaShin-ichi, YamashitaSeigo, TokudaMichifumi, YoshidaHiroshi, InadaKeiichi, ShibayamaKenri, MiyanagaSatoru, MiyazakiHidekazu, AbeKunihiko, SugimotoKen-ichi, YoshimuraMichihiro. Repeated provocation of time- and ATP-induced early pulmonary vein reconnections after pulmonary vein isolation: eliminating paroxysmal atrial fibrillation in a single procedure. Circ Arrhythm Electrophysiol. 2011;4 (5):601–8.
86. Kasai A, AnselmeF, TeoW S, CribierA, SaoudiN. Comparison of effectiveness of an 8-mm versus a 4-mm tip electrode catheter for radiofrequency ablation of typical atrial flutter. Am. J. Cardiol. 2000;86 (9):1029–32, A10.
87. Schreieck Juergen, ZrennerBernhard, KumpmannJohanna, NdrepepaGjin, SchneiderMichael A E, DeisenhoferIsabel, SchmittClaus. Prospective randomized comparison of closed cooled-tip versus 8-mm-tip catheters for radiofrequency ablation of typical atrial flutter. J. Cardiovasc. Electrophysiol. 2002;13 (10):980–5.
88. Andrade Jason G, KhairyPaul, GuerraPeter G, DeyellMarc W, RivardLena, MacleLaurent, ThibaultBernard, TalajicMario, RoyDenis, DubucMarc. Efficacy and safety of cryoballoon ablation for atrial fibrillation: a systematic review of published studies. Heart Rhythm. 2011;8 (9):1444–51.
89. Khairy Paul, ChauvetPatrick, LehmannJohn, LambertJean, MacleLaurent, TanguayJean-François, SiroisMartin G, SantoianniDomenic, DubucMarc. Lower incidence of thrombus formation with cryoenergy versus radiofrequency catheter ablation. Circulation. 2003;107 (15):2045–50.
90. Chierchia Gian Battista, CapulziniLucio, DroogmansSteven, SorgenteAntonio, SarkozyAndrea, Müller-BurriAndreas, PaparellaGaetano, de AsmundisCarlo, YazakiYoshinao, KerkhoveDirk, Van CampGuy, BrugadaPedro. Pericardial effusion in atrial fibrillation ablation: a comparison between cryoballoon and radiofrequency pulmonary vein isolation. Europace. 2010;12 (3):337–41.
91. Yu W C, HsuT L, TaiC T, TsaiC F, HsiehM H, LinW S, LinY K, TsaoH M, DingY A, ChangM S, ChenS A. Acquired pulmonary vein stenosis after radiofrequency catheter ablation of paroxysmal atrial fibrillation. J. Cardiovasc. Electrophysiol. 2001;12 (8):887–92.
92. Avitall Boaz, UrbonieneDalia, RozmusGrzegorz, LafontaineDan, HelmsRay, UrbonasArvydas. New cryotechnology for electrical isolation of the pulmonary veins. J. Cardiovasc. Electrophysiol. 2003;14 (3):281–6.
93. Ahmed Humera, NeuzilPetr, d'AvilaAndre, ChaYong-Mei, LaragyMargaret, MaresKarel, BruggeWilliam R, ForcioneDavid G, RuskinJeremy N, PackerDouglas L, ReddyVivek Y. The esophageal effects of cryoenergy during cryoablation for atrial fibrillation. Heart Rhythm. 2009;6 (7):962–9.
94. Metzner Andreas, ChunK R Julian, NevenKars, FuernkranzAlexander, OuyangFeifan, AntzMatthias, TilzRoland, ZermThomas, KoektuerkBuelent, WissnerEric, KoesterIlka, ErnstSabine, BoczorSigrid, KuckKarl-Heinz, SchmidtBoris. Long-term clinical outcome following pulmonary vein isolation with high-intensity focused ultrasound balloon catheters in patients with paroxysmal atrial fibrillation. Europace. 2010;12 (2):188–93.
95. Metzner Andreas, SchmidtBoris, FuernkranzAlexander, WissnerErik, TilzRoland R, ChunK R Julian, NevenKars, KonstantinidouMelanie, RilligAndreas, YoshigaYazuhiro, MathewShibu, KoesterIlka, OuyangFeifan, KuckKarl-Heinz. One-year clinical outcome after pulmonary vein isolation using the novel endoscopic ablation system in patients with paroxysmal atrial fibrillation. Heart Rhythm. 2011;8 (7):988–93.
96. Mulder Anton A W, WijffelsMaurits C E F, WeverEric F D, BoersmaLucas V A. Pulmonary vein anatomy and long-term outcome after multi-electrode pulmonary vein isolation with phased radiofrequency energy for paroxysmal atrial fibrillation. Europace. 2011;13 (11):1557–61.
97. Mulder Anton A W, WijffelsMaurits C E F, WeverEric F D, BoersmaLucas V A. Pulmonary vein isolation and left atrial complex-fractionated atrial electrograms ablation for persistent atrial fibrillation with phased radio frequency energy and multi-electrode catheters: efficacy and safety during 12 months follow-up. Europace. 2011;13 (12):1695–702.
98. Stabile Giuseppe, De RuvoErmenegildo, GrimaldiMassimo, RovarisGiovanni, SoldatiEzio, AnselminoMatteo, SolimeneFrancesco, IulianoAssunta, SciarraLuigi, SchillaciVincenzo, BongiorniMaria Grazia, GaitaFiorenzo, CalòLeonardo. Safety and efficacy of pulmonary vein isolation using a circular, open-irrigated mapping and ablation catheter: A multicenter registry. Heart Rhythm. 2015;12 (8):1782–8.
99. Mahida Saagar, HooksDarren A, NentwichKarin, NgG Andre, GrimaldiMassimo, ShinDong-In, DervalNicolas, SacherFrederic, BerteBenjamin, YamashitaSeigo, DenisArnaud, HociniMélèze, DenekeThomas, HaissaguerreMichel, JaisPierre. nMARQ Ablation for Atrial Fibrillation: Results from a Multicenter Study. J. Cardiovasc. Electrophysiol. 2015;26 (7):724–9.
100. Gaita Fiorenzo, LeclercqJean François, SchumacherBurghard, ScaglioneMarco, TosoElisabetta, HalimiFranck, SchadeAnja, FroehnerSteffen, ZieglerVolker, SergiDomenico, CesaraniFederico, BlandinoAlessandro. Incidence of silent cerebral thromboembolic lesions after atrial fibrillation ablation may change according to technology used: comparison of irrigated radiofrequency, multipolar nonirrigated catheter and cryoballoon. J. Cardiovasc. Electrophysiol. 2011;22 (9):961–8.
101. Herrera Siklódy Claudia, DenekeThomas, HociniMélèze, LehrmannHeiko, ShinDong-In, MiyazakiShinsuke, HenschkeSusanne, FluegelPeter, Schiebeling-RömerJochen, BansmannPaul M, BourdiasThomas, DoussetVincent, HaïssaguerreMichel, ArentzThomas. Incidence of asymptomatic intracranial embolic events after pulmonary vein isolation: comparison of different atrial fibrillation ablation technologies in a multicenter study. J. Am. Coll. Cardiol. 2011;58 (7):681–8.
102. Scaglione Marco, BiascoLuigi, CaponiDomenico, AnselminoMatteo, NegroAndrea, Di DonnaPaolo, CorletoAntonella, MontefuscoAntonio, GaitaFiorenzo. Visualization of multiple catheters with electroanatomical mapping reduces X-ray exposure during atrial fibrillation ablation. Europace. 2011;13 (7):955–62.
103. Estner Heidi Luise, DeisenhoferIsabel, LuikArmin, NdrepepaGjin, von BaryChristian, ZrennerBernhard, SchmittClaus. Electrical isolation of pulmonary veins in patients with atrial fibrillation: reduction of fluoroscopy exposure and procedure duration by the use of a non-fluoroscopic navigation system (NavX). Europace. 2006;8 (8):583–7.
104. Dong Jun, DickfeldTimm, DalalDarshan, CheemaAamir, VasamreddyChandrasekhar R, HenriksonCharles A, MarineJoseph E, HalperinHenry R, BergerRonald D, LimaJoao A C, BluemkeDavid A, CalkinsHugh. Initial experience in the use of integrated electroanatomic mapping with three-dimensional MR/CT images to guide catheter ablation of atrial fibrillation. J. Cardiovasc. Electrophysiol. 2006;17 (5):459–66.
105. Bulava Alan, HanisJiri, EisenbergerMartin. Catheter Ablation of Atrial Fibrillation Using Zero-Fluoroscopy Technique: A Randomized Trial. Pacing Clin Electrophysiol. 2015;38 (7):797–806.
106. Bertaglia Emanuele, BellaPaolo Della, TondoClaudio, ProclemerAlessandro, BottoniNicola, De PontiRoberto, LandolinaMaurizio, BongiorniMaria Grazia, CoròLeonardo, StabileGiuseppe, Dello RussoAntonio, VerlatoRoberto, ManticaMassimo, ZoppoFranco. Image integration increases efficacy of paroxysmal atrial fibrillation catheter ablation: results from the CartoMerge Italian Registry. Europace. 2009;11 (8):1004–10.
107. Kistler Peter M, RajappanKim, HarrisStuart, EarleyMark J, RichmondLaura, SportonSimon C, SchillingRichard J. The impact of image integration on catheter ablation of atrial fibrillation using electroanatomic mapping: a prospective randomized study. Eur. Heart J. 2008;29 (24):3029–36.
108. Caponi Domenico, CorletoAntonella, ScaglioneMarco, BlandinoAlessandro,

BiascoLuigi, CristoforettiYvonne, CerratoNatascia, TosoElisabetta, MorelloMara, GaitaFiorenzo. Ablation of atrial fibrillation: does the addition of three-dimensional magnetic resonance imaging of the left atrium to electroanatomic mapping improve the clinical outcome?: a randomized comparison of Carto-Merge vs. Carto-XP three-dimensional mapping ablation in patients with paroxysmal and persistent atrial fibrillation. Europace. 2010;12 (8):1098–104.

109. Di Biase Luigi, BurkhardtJ David, MohantyPrasant, SanchezJavier, HortonRodney, GallinghouseG Joseph, LakkireddyDhanunjay, VermaAtul, KhaykinYaariv, HongoRichard, HaoSteven, BeheirySalwa, PelargonioGemma, Dello RussoAntonio, CasellaMichela, SantarelliPietro, SantangeliPasquale, WangPaul, Al-AhmadAmin, PatelDimpi, ThemistoclakisSakis, BonsoAldo, RossilloAntonio, CorradoAndrea, RavieleAntonio, CummingsJennifer E, SchweikertRobert A, LewisWilliam R, NataleAndrea. Periprocedural stroke and management of major bleeding complications in patients undergoing catheter ablation of atrial fibrillation: the impact of periprocedural therapeutic international normalized ratio. Circulation. 2010;121 (23):2550–6.
110. Lakkireddy Dhanunjaya, ReddyYeruva Madhu, Di BiaseLuigi, VangaSubba Reddy, SantangeliPasquale, SwarupVijay, PimentelRhea, MansourMoussa C, D'AvilaAndre, SanchezJavier E, BurkhardtJ David, ChalhoubFadi, MohantyPrasant, CoffeyJames, ShaikNaushad, MonirGeorge, ReddyVivek Y, RuskinJeremy, NataleAndrea. Feasibility and safety of dabigatran versus warfarin for periprocedural anticoagulation in patients undergoing radiofrequency ablation for atrial fibrillation: results from a multicenter prospective registry. J. Am. Coll. Cardiol. 2012;59 (13):1168–74.
111. Cappato Riccardo, MarchlinskiFrancis E, HohnloserStefan H, NaccarelliGerald V, XiangJim, WilberDavid J, MaChang-Sheng, HessSusanne, WellsDarryl S, JuangGeorge, VijgenJohan, HüglBurkhard J, BalasubramaniamRichard, De ChillouChristian, DaviesD Wyn, FieldsL Eugene, NataleAndrea. Uninterrupted rivaroxaban vs. uninterrupted vitamin K antagonists for catheter ablation in non-valvular atrial fibrillation. Eur. Heart J. 2015;36 (28):1805–11.
112. Gurses Kadri Murat, KocyigitDuygu, YalcinMuhammed Ulvi, EvranosBanu, YorgunHikmet, SahinerMehmet Levent, KayaErgun Baris, OtoMehmet Ali, OzerNecla, AytemirKudret. Safety and efficacy outcomes of protamine administration for heparin reversal following cryoballoon-based pulmonary vein isolation. J Interv Card Electrophysiol. 2015;43 (2):161–7.
113. Patel Aarti A, ClyneChristopher A, HenyanNickole N, WhiteC Michael, ZembrowskiBryan F, MigeedMagdy, YarlagaddaRavi, KlugerJeffrey, ColemanCraig I. The use of protamine after radiofrequency catheter ablation: a pilot study. J Interv Card Electrophysiol. 2007;18 (2):155–8.
114. Conte Giulio, de AsmundisCarlo, BaltogiannisGiannis, Di GiovanniGiacomo, CiconteGiuseppe, SieiraJuan, SaitohYukio, WautersKristel, MugnaiGiacomo, JuliàJusto, IrfanGhazala, LevinsteinMoises, Cotino-MorenoHugo Enrique, ChierchiaGian-Battista, BrugadaPedro. Periprocedural outcomes of prophylactic protamine administration for reversal of heparin after cryoballoon ablation of atrial fibrillation. J Interv Card Electrophysiol. 2014;41 (2):129–34.
115. Noheria Amit, KumarAbhishek, WylieJohn V, JosephsonMark E. Catheter ablation vs antiarrhythmic drug therapy for atrial fibrillation: a systematic review. Arch. Intern. Med. 2008;168 (6):581–6.
116. Cosedis Nielsen Jens, JohannessenArne, RaatikainenPekka, HindricksGerhard, WalfridssonHåkan, KongstadOle, PehrsonSteen, EnglundAnders, HartikainenJuha, MortensenLeif Spange, HansenPeter Steen. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation. N. Engl. J. Med. 2012;367 (17):1587–95.
117. Takigawa Masateru, TakahashiAtsushi, KuwaharaTaishi, OkuboKenji, TakahashiYoshihide, WatariYuji, TakagiKatsumasa, FujinoTadashi, KimuraShigeki, HikitaHiroyuki, TomitaMakoto, HiraoKenzo, IsobeMitsuaki. Long-term follow-up after catheter ablation of paroxysmal atrial fibrillation: the incidence of recurrence and progression of atrial fibrillation. Circ Arrhythm Electrophysiol. 2014;7 (2):267–73.
118. Packer Douglas L, KowalRobert C, WheelanKevin R, IrwinJames M, ChampagneJean, GuerraPeter G, DubucMarc, ReddyVivek, NelsonLinda, HolcombRichard G, LehmannJohn W, RuskinJeremy N. 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. 2013;61 (16):1713–23.
119. Hummel John, MichaudGregory, HoytRobert, DeLurgioDavid, RasekhAbdi, KusumotoFred, GiudiciMichael, DanDan, TschoppDavid, CalkinsHugh, BoersmaLucas. Phased RF ablation in persistent atrial fibrillation. Heart Rhythm. 2014;11 (2):202–9.
120. Aytemir Kudret, GursesKadri Murat, YalcinMuhammed Ulvi, KocyigitDuygu, DuralMuhammet, EvranosBanu, YorgunHikmet, AtesAhmet Hakan, SahinerMehmet Levent, KayaErgun Baris, OtoMehmet Ali. Safety and efficacy outcomes in patients undergoing pulmonary vein isolation with second-generation cryoballoon†. Europace. 2015;17 (3):379–87.
121. Straube Florian, DorwarthUwe, SchmidtMartin, WankerlMichael, EbersbergerUlrich, HoffmannEllen. Comparison of the first and second cryoballoon: high-volume single-center safety and efficacy analysis. Circ Arrhythm Electrophysiol. 2014;7 (2):293–9.
122. Di Giovanni Giacomo, WautersKristel, ChierchiaGian-Battista, SieiraJuan, LevinsteinMoises, ConteGiulio, de AsmundisCarlo, BaltogiannisGiannis, SaitohYukio, CiconteGiuseppe, JuliaJusto, MugnaiGiacomo, IrfanGhazala, BrugadaPedro. One-year follow-up after single procedure Cryoballoon ablation: a comparison between the first and second generation balloon. J. Cardiovasc. Electrophysiol. 2014;25 (8):834–9.
123. Fürnkranz Alexander, BordignonStefano, DugoDaniela, PerottaLaura, GunawardeneMelanie, Schulte-HahnBritta, NowakBernd, SchmidtBoris, ChunJulian K R. Improved 1-year clinical success rate of pulmonary vein isolation with the second-generation cryoballoon in patients with paroxysmal atrial fibrillation. J. Cardiovasc. Electrophysiol. 2014;25 (8):840–4.
124. Metzner Andreas, ReissmannBruno, RauschPeter, MathewShibu, WohlmuthPeter, TilzRoland, RilligAndreas, LemesChristine, DeissSebastian, HeegerChristian, KamiokaMasashi, LinTina, OuyangFeifan, KuckKarl-Heinz, WissnerErik. One-year clinical outcome after pulmonary vein isolation using the second-generation 28-mm cryoballoon. Circ Arrhythm Electrophysiol. 2014;7 (2):288–92.
125. Mugnai Giacomo, ChierchiaGian-Battista, de AsmundisCarlo, Sieira-MoretJuan, ConteGiulio, CapulziniLucio, WautersKristel, Rodriguez-MañeroMoises, Di GiovanniGiacomo, BaltogiannisGiannis, CiconteGiuseppe, SaitohYukio, JuliáJusto, BrugadaPedro. Comparison of pulmonary vein isolation using cryoballoon versus conventional radiofrequency for paroxysmal atrial fibrillation. Am. J. Cardiol. 2014;113 (9):1509–13.
126. Wasserlauf Jeremiah, PelchovitzDaniel J, RhynerJohn, VermaNishant, BohnMartha, LiZhi, AroraRishi, ChicosAlexandru B, GoldbergerJeffrey J, KimSusan S, LinAlbert C, KnightBradley P, PassmanRod S. Cryoballoon versus radiofrequency catheter ablation for paroxysmal atrial fibrillation. Pacing Clin Electrophysiol. 2015;38 (4):483–9.
127. Aryana Arash, SinghSheldon M, KowalskiMarcin, PujaraDeep K, CohenAndrew I, SinghSteve K, AleongRyan G, BankerRajesh S, FuenzalidaCharles E, PragerNelson A, BowersMark R, D'AvilaAndré, O'NeillPadraig Gearoid. 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. 2015;26 (8):832–9.
128. Brooks Anthony G, StilesMartin K, LaborderieJulien, LauDennis H, KuklikPawel, ShippNicholas J, HsuLi-Fern, SandersPrashanthan. Outcomes of long-standing persistent atrial fibrillation ablation: a systematic review. Heart Rhythm. 2010;7 (6):835–46.

129. Wynn Gareth J, DasMoloy, BonnettLaura J, PanikkerSandeep, WongTom, GuptaDhiraj. Efficacy of catheter ablation for persistent atrial fibrillation: a systematic review and meta-analysis of evidence from randomized and nonrandomized controlled trials. Circ Arrhythm Electrophysiol. 2014;7 (5):841–52.

130. Ouyang Feifan, TilzRoland, ChunJulian, SchmidtBoris, WissnerErik, ZermThomas, NevenKars, KöktürkBulent, KonstantinidouMelanie, MetznerAndreas, FuernkranzAlexander, KuckKarl-Heinz. Long-term results of catheter ablation in paroxysmal atrial fibrillation: lessons from a 5-year follow-up. Circulation. 2010;122 (23):2368–77.

131. Medi C, SparksP B, MortonJ B, KistlerP M, HalloranK, RossoR, VohraJ K, KumarS, KalmanJ M. Pulmonary vein antral isolation for paroxysmal atrial fibrillation: results from long-term follow-up. J. Cardiovasc. Electrophysiol. 2011;22 (2):137–41.

132. Oral Hakan, PapponeCarlo, ChughAman, GoodEric, BogunFrank, PelosiFrank, BatesEric R, LehmannMichael H, VicedominiGabriele, AugelloGiuseppe, AgricolaEustachio, SalaSimone, SantinelliVincenzo, MoradyFred. Circumferential pulmonary-vein ablation for chronic atrial fibrillation. N. Engl. J. Med. 2006;354 (9):934–41.

133. Wynn Gareth J, DasMoloy, BonnettLaura J, GuptaDhiraj. Quality-of-life benefits of catheter ablation of persistent atrial fibrillation: a reanalysis of data from the SARA study. Europace. 2015;17 (2):222–4.