Review

Ablation of Atrial Fibrillation: Patient Selection, Techniques, and the Outcome

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Introduction

Atrial fibrillation (AF) is a common arrhythmia, affecting an estimated 2 million people in the United States (Table 1). The data from the Framingham indicate that the prevalence of AF increases with age, affecting as many as 4% of people 60 to 65 years of age, and 10% of those ≥ 80 years. AF can occur in the absence of underlying heart disease but is more frequent in connection with mitral valve disorder, heart failure, ischemic heart disease, and hypertension. In addition to the devastating symptoms, AF confers a four to five-fold increase in the risk of stroke compared to the general population; a significant risk of tachycardia mediated cardiomyopathy that has been associated with a doubling of all causes of mortality.[1] During the past decade, limited success rates of drug treatment stimulated an exploration of interventional treatment options for AF. [2]

Jaïs et al. recently conducted a randomized comparison of catheter ablation and antiarrhythmic treatment strategies in patients with paroxysmal AF resistant to at least one antiarrhythmic drug.[3] One hundred and twelve patients (aged 51.1±11.1 years) were randomized to ablation (n=53) or new antiarrhythmic drugs alone or in combination (n=59). Crossover from the antiarrhythmic drugs and ablation groups occurred in 37 (63%) and 5 patients (9%), respectively (P<0.0001). In one year follow-up, 13 of 55 patients (23%) and 46 of 52 patients (89%) had no recurrence of AF in the antiarrhythmic drug and ablation groups, respectively (P<0.0001). Symptom score, exercise capacity, and quality of life were significantly higher in the ablation group.[3]

As our knowledge on initiating triggers and perpetuating substrate of AF expanded, different potentially curative catheter ablation techniques have developed. The goals of AF ablation are elimination of symptoms and improvement in quality of life, prevention of complications and, potential improvement in survival.[2]

Catheter ablation has now emerged as a treatment strategy to target pulmonary venous triggers that initiate paroxysmal AF.[4] The feasibility of catheter ablation has been demonstrated for patients with paroxysmal to permanent AF. There are recent data to support the role of catheter ablation in patients with persistent and permanent AF and especially those with left ventricular dysfunction.[5-11]

Patient selection

Elimination of symptoms and improvement in quality of life; prevention of complica-

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Table 1: definition of atrial fibrillation.

Type of AF	Definition
Paroxysmal	Paroxysmal AF is defined as recurrent AF (2 episodes) that terminates spontaneously within 7 days.
Persistent	Persistent AF is sustained beyond seven days, or lasting less than seven days but necessitating pharmacologic or electrical cardioversion. Longstanding persistent AF is defined as continuous AF of greater than one-year duration.
Permanent	The term permanent AF refers to a group of patients where a decision has been made *not* to pursue restoration of sinus rhythm by any means, including catheter or surgical ablation.

AF: atrial fibrillation

tions such as thromboembolic events; and, at least in theory, improvement in survival are the therapy targets in AF. As demonstrated in published studies, the primary clinical benefit from catheter ablation of AF is an improvement in quality of life resulting from elimination of arrhythmia-related symptoms. Thus, the primary selection criterion for catheter ablation should be the presence of *symptomatic* AF refractory or intolerant to a Class I or III antiarrhythmic medication. However, despite the lack of data, asymptomatic patients can be considered for catheter ablation if they are young and/or have evidence of a possible tachycardia-mediated cardiomyopathy.[2,11,12] Patients with congestive heart failure and left ventricular dysfunction should also be considered for left atrial catheter ablation, a procedure proved to be feasible and clinically efficient.[11,12]

Khan et al. randomly assigned patients with symptomatic, drug-resistant AF, an ejection fraction of 40% or less, and NYHA class II or III heart failure to undergo either pulmonary-vein isolation (n=41) or atrioventricular-node ablation (n=40) with biventricular pacing.[12] At six months 88% of patients in the pulmonary-vein isolation group cured from AF with or without the use of antiarrhythmic medications. The ejection fraction improved in 76% of patients who underwent pulmonary-vein isolation but in only 25% of patients who underwent atrioventricular-node ablation with biventricular pacing. In the group that underwent pulmonary-vein isolation, the distance increased from 269±54 meters at baseline to 340±49 meters at 6 months, as compared with 281±44 meters to 297±36 meters at 6 months in the group that underwent atrioventricular-node ablation with biventricular pacing (P<0.001).[12]

A comparable efficacy is usually achieved in older patients, however the risk of complications, especially tamponade and thromboembolic events, may be higher in these patients. In one study, the efficacy of left atrial catheter ablation was similar among patients with AF who were ≤70 years and over. However, the incidence of tamponade and thromboembolic events was four times higher in patients aged >70 years than in those ≤70 years.[13] However other studies showed comparable complication rates.[14] Corraddo et al studied 174 consecutive patients > 75 years of age who underwent AF ablation. AF was er a mean follow-up of 20 ± 14 paroxysmal in 55% and high-risk $CHADS_2$ score (≥2) was present in 65% of the population. Ovmonths, 127 (73%) maintained sinus rhythm with a single procedure, whereas 47 patients had recurrence of AF. Of these 20 patients had a second ablation, successful in 16 (80%).[14] During the follow-up, three patients had a CVA within the first 6 weeks after ablation. Warfarin was discontinued in 138 out of 143 pa-

Table 2: prevalence of major complications in 1600 atrial fibrillation ablation in Leipzig's Heart Center between January 2002 – October 2007.

Complications	Number	Percent
Periprocedural death	0	0.00%
Tamponade	10	0.60%
Stroke/transient ischemic attack	5	0.30%
Air embolism	1	0.06%
Pulmonary embolism	2	0.12%
Vascular complications	14	0.82%
Pulmonary vein stenosis	5	0.30%
Atrioesophageal fistula	2	0.12%
Phrenic nerve paresis	0	0.00%
Pneumo- or Hemothorax	0	0.00%
Total	39	~2.3%

tients (96%) who maintained SR without antiarrhythmic medications with no embolic event occurring over a mean follow-up of 16 ± 12 months.[14]

Nademanee et al. performed AF substrate ablation guided by complex fractionated atrial electrogram mapping in 674 high-risk AF patients in order to assess the potential effect of catheter ablation on mortality. [15] After the mean follow-up period of 836 ± 605 days, 517 were in sinus rhythm (81.4%). There were 15 deaths among the patients who stayed in sinus rhythm compared with 14 deaths in those who remained in AF (5-year survival rate, 92% vs. 64%, respectively; $p < 0.0001$). Sinus rhythm after catheter ablation was the most important independent favorable parameter for survival (hazard ratio 0.14, 95% confidence interval 0.06 to 0.36, $p < 0.0001$).

Left atrial size should be considered in the process of patient selection for the catheter ablation of atrial fibrillation. A left atrial diameter > 50 to 55 mm predicts a lower probability of a successful outcome. A dilated left atrium is likely to be associated with substantial electroanatomic remodeling, and this may decrease the probability of a successful ablation. [2] A long duration of AF from the time of first diagnosis in patients with chronic AF may be associated with a higher probability of recurrent AF after ablation. However, a cutoff value for the duration of AF has not been reported. In patients with paroxysmal AF, the duration of AF does not appear to be a predictor of outcome.[2]

In clinical practice, many patients with asymptomatic AF seek catheter ablation as an alternative to long-term anticoagulation therapy with warfarin. However, it should be emphasized that this concept has never been confirmed by a large prospective randomized clinical trial and therefore remains unverified. Therefore A patient's desire to eliminate the need for long-term anticoagulation by itself should not be considered an appropriate selection criterion.[12] Warfarin is recommended for all patients for at least three months following an AF ablation procedure. Decisions regarding the use of warfarin more than three months following ablation should be based on the patient's risk factors for stroke and not on the presence or type of AF.

In conclusion the ideal candidate for catheter ablation of AF has symptomatic episodes of

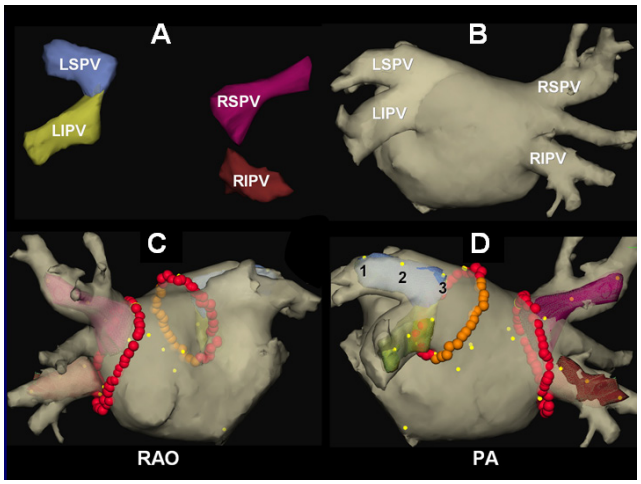

Figure 1. Shows the procedural steps for ablation of AF in a patient with paroxysmal AF using EnSite-NavX system. The first step is the reconstruction of pulmonary veins (A). Using fiducial points in pulmonary veins and left atrium (yellow points in C and D) the reconstructed left atrium (B) is registered and then used for the ablation procedure. C and D show the final circumferential ablation lesions (red and orange dots) around the left and right pulmonary veins in RAO and PA views, respectively. **LIPV:** left inferior pulmonary vein; **LSPV:** left superior pulmonary vein; **RIPV:** right inferior pulmonary vein; **RSPV:** right superior pulmonary vein, **PA:** posteroanterior; **RAO:** right anterior oblique.

paroxysmal or persistent AF, has not responded to one antiarrhythmic drugs, does not have severe comorbidities or significant structural heart disease, is younger than 70-75 years, has a left atrial <55 mm, and, for chronic AF, has had AF for <5 years.[2] However, with improvement of ablation techniques, the threshold for ablation will continue to fall especially in young patients and those with left ventricular dysfunction.

Techniques for and endpoints of catheter ablation of AF

segmental pulmonary vein (PV) isolation was introduced by Haissaguerre et al.[3] The technique involved identification and ablation of the earliest sites of activation of the PV musculature at the PV ostium. This usually resulted in the delivery of RF energy to 30% to 80% of the circumference of the PVs. [3] The endpoint of this procedure at our center is complete bidirectional electrical isolation of all PVs.[12]

The recognition of PV stenosis as a complication of RF delivery within a PV, as well as the recognition of the importance of PV antrum in initiation and maintenance of AF, resulted in a shift in ablation strategies. This would target the atrial antral tissue rather than the PV itself. Moreover, an anatomically based ablation strategy of circumferential PV isolation and ablation guided by three dimensional electroanatomical mapping was subsequently developed by Pappone and his colleagues (Fig. 1 and 2).[12,13] Different centers use various endpoints for this procedure including amplitude reduction within the ablated area, elimination (or dissociation) of the PV potentials recorded within the ipsilateral PVs, and/or complete isolation and exit block from the PV.[12]

Although PV isolation based ablation strategies, especially circumferential PV isolation remain the cornerstone of AF ablation procedures for both paroxysmal and persistent AF, additive strategies are developed to improve the outcome in patients with persistent AF. One of these strategies is to create additional linear

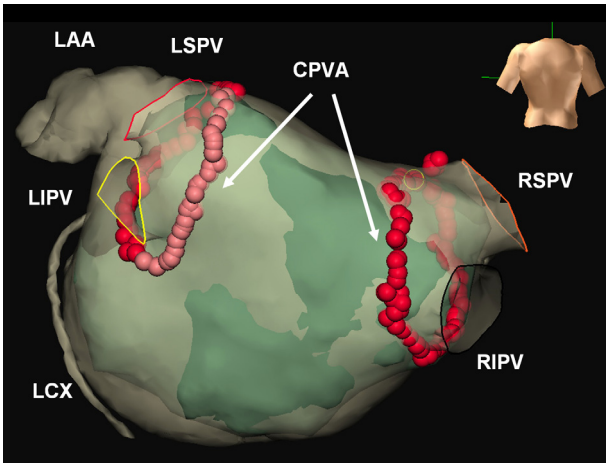

Figure 2. Posteroanterior view of the reconstructed (green area) left atrium merged with segmented left atrium from computed tomography after the AF ablation procedure in a patient with paroxysmal AF using EnSite-NavX system. The red dots show the ablation lesions. The pink points show the titrated power application based on the temperature measurement in esophagus. **CPVA:** circumferential pulmonary vein ablation; **LAA:** left atrial appendage; **LCX:** left circumflex artery; **LIPV:** left inferior pulmonary vein; **LSPV:** left superior pulmonary vein; **RIPV:** right inferior pulmonary vein; **RSPV:** right superior pulmonary vein.

lesions with the endpoint of complete bidirectional block in the left atrium (Fig. 3). The most common linear lesions are the left atrial "roof" line connecting the superior aspects of the left and right PV circumferential lesions. Also complete isolation of the posterior wall with a "Box Lesion", the region of tissue between the mitral valve and the left inferior PV (the mitral isthmus), and anteriorly between the roof line near the left or right circumferential lesion and the mitral annulus.[12] In selected patients especially those with longstanding (i.e. AF > 1 year) persistent AF, other ablation strategies including ablation of non PV triggers, areas with com-

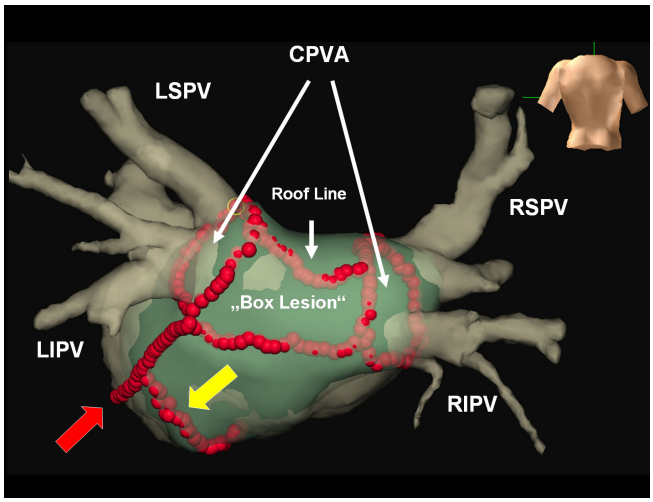

Figure 3. Posteroanterior view of the reconstructed (green area) left atrium merged with segmented left atrium from computed tomography after the AF ablation procedure in a patient with permanent AF using EnSite-NavX system. The aim of the "Box Lesion" is the complete isolation and electrical silence of the posterior left atrium. The red arrow represent the mitral isthmus line. The yellow arrow represent the linear endocardial ablation along the coronary sinus. **CPVA:** circumferential pulmonary vein ablation; **LIPV:** left inferior pulmonary vein; **LSPV:** left superior pulmonary vein; **RIPV:** right inferior pulmonary vein; **RSPV:** right superior pulmonary vein.

plex fractionated atrial electrograms, coronary sinus, ganglion plexus, and linear lesions in right atrium can improve the long term results.[12] In patients with longstanding persistent AF, a step-wise approach to ablation has been proposed and reported to be successful in >80% of patients.[5, 9] Finally ablation of the cavotricuspid isthmus is recommended in patients with a history of typical atrial flutter or inducible cavotricuspid isthmus dependent atrial flutter.

There are three principal end points recommended for catheter ablation of AF, the applicability and relevance of which may depend on the type of AF. These include PV isolation and completion of a predetermined lesion set, termination of AF during ablation, and noninducibility of AF after ablation. However, it is still unclear if endpoints of termination and especially non-inducibility of AF are necessary or even feasible especially in patients with persistent AF. However, in cases of organized atrial tachycardias and flutters, termination and noninducibility should be considered as plausible endpoints.

The endpoint of noninducibility seems to be important also in patients with paroxysmal AF. [21] Haïssaguerre et al. studied 70 patients with paroxysmal AF. PV isolation terminated AF in 75% of patients. Sustained AF was noninducible in 57% after PV isolation and in 77% after linear ablation. At 7±3 months, 74% with PV isolation and 83% with linear ablation were arrhythmia free without antiarrhythmic medication, which was significantly associated with noninducibility (P=0.03) with a recurrence rate of 38% and 13% in patients with and without inducibility, respectively. [21]

Outcomes of catheter ablation of AF

Inconsistent treatment results made judging the efficacy of the individual ablation strategies difficult. Apart from differences in patient selection, and ablation technique, the varying results could also partly be due to differences in the follow-up duration and strategy and definition of the success.[14] The bulk of evidence suggests that presence or absence of symptoms does not affect the prognosis and complications of the AF. The emerging data show that asymptomatic AF occurs frequently after catheter ablation, even in the patients with highly symptomatic AF before the ablation procedure. In addition, the number of patients with episodes of the asymptomatic AF actually increases after catheter ablation of AF. This would at least in part explain the apparent discrepancy between reported outcomes in various clinical studies on catheter ablation of AF. Therefore, objective follow-up strategies with repetitive, long-term, Holter monitoring devices or implantable loop recorders are necessary to analyze rhythm outcome after the catheter ablation of AF.[14]

Recurrence of AF is common early (< 1 month) following catheter ablation and occurs regardless of the catheter technique used in up to 45% of patients. The incidence of early recurrence is higher in patients with persistent AF, older patients (>65 years), and those with concomitant structural heart disease.[12] Although early recurrence of AF is an independent predictor of treatment failure, its occurrence should not prompt immediate re-ablation attempts as 60% of patients experiencing this event within the first months post-ablation will not have any further arrhythmias during long-term follow-up.

Currently the rate of late recurrence (up to 12 month after ablation) in patients with paroxysmal and persistent AF is 10-20% and 20-

30%, respectively. Furthermore, the very late recurrence (more than 12 months) after catheter ablation occurs in approximately 5% to 10% of patients. Are the patients with asymptomatic AF recurrence candidates for repeat ablation of AF?. Catheter ablation to eliminate AF in totally asymptomatic patients may not be appropriate until large, randomized, long-term evidenced-based studies, which are urgently needed, become available. However asymptomatic patients can be considered for catheter ablation if they have evidence of a possible tachycardia-induced cardiomyopathy and left ventricular dysfunction.[18]

Ablation of AF is one of the most complicated procedures in the interventional electrophysiology and therefore the rate of complications is higher than conventional ablation procedures. The world-wide survey of AF ablation reported that at least one major complication was seen in 6% of patients with only four early deaths recorded in 8,745 patients.[19] However, the rate of major complication varies widely between centers. Table 1 summarizes the complications occurred during 1600 AF ablations at our center (Phillip Sommer: personal communication). In conclusion during the past decade, limited success rates of drug treatment stimulated an exploration of interventional treatment options for AF and it is clear now that catheter ablation has moved into the mainstream of electrophysiological management of AF. The ideal candidate for catheter ablation of AF shows symptomatic episodes of paroxysmal or persistent AF, has not responded to one antiarrhythmic drugs, does not have severe co-morbidities, is younger than 70-75 years, has a left atrial <55 mm, and, for chronic AF, has had AF for <5 years. However, with improvement of ablation techniques, the threshold for ablation will continue to fall. Asymptomatic patients can be considered for catheter ablation if they have evidence of a possible tachycardia-induced cardiomyopathy and left ventricular dysfunction.

In the hands of experienced operators, AF ablation is an effective and safe treatment for AF and offers an excellent chance for a long term cure. Therefore as some experienced electrophysiologist believe it is about time that AF ablation be used as a first-line option for selected patients with AF.[20]

Conflicts of Interest no declare.

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