Catheter Ablation of Atrial Fibrillation – Techniques and Technology

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Abstract

For certain patients with atrial fibrillation (AF) catheter ablation is now an important, therapeutic, intervention. It is established that catheter ablation is more effective than antiarrhythmic drug therapy at maintaining middle-aged patients with paroxysmal AF in sinus rhythm. However, the role of catheter ablation in other patient groups is not yet well defined. Particularly in patients with long-standing persistent AF, heart failure and the elderly, the efficacy of catheter ablation remains uncertain. At experienced centers catheter ablation for AF can be performed with reasonable safety and efficacy. However, major complications can occasionally occur. Late recurrence of AF is not uncommon and many patients will require a further procedure to maintain sinus rhythm. Fortunately, there are promising developments in the techniques and technology used for AF ablation that are likely to improve the outcomes of the procedure.

Keywords

Catheter ablation, atrial fibrillation (AF), antiarrhythmic drug therapy, heart failure

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Over the past decades catheter ablation of atrial fibrillation (AF) has evolved from being a largely experimental procedure to a well-established therapeutic option for certain patients with AF.^{1–4} Currently the backbone of most catheter ablation techniques is to target the pulmonary veins (PVs) in order to achieve their electrical isolation and maintain sinus rhythm (SR).¹ Additional techniques may be used to ablate non-PV triggers and candidate atrial sites considered responsible for maintaining AF.¹

Drawing upon our experience and our literature review, we would estimate the single procedure efficacy of AF ablation in an “optimal” candidate for AF ablation to be between 60 % and 80 %. The single procedure in a less optimal patient, such as a patient with persistent AF, lies between 50 % and 70 %. The single efficiency of the procedure in a suboptimal patient, such as a patient with continuous AF for four years, is 40 % or less. It is important to recognise that AF may recur following ablation and that patients may need a second procedure for which the success rate is cumulative.

In this paper we will initially describe the reasons why we may consider catheter ablation as a treatment for AF. We will then discuss the current ways by which catheter ablation for AF is performed. We will review the relative efficiency of ablation compared to other treatment options. Finally, we will discuss what the future may hold for AF ablation procedures and how these may impact on current success rates and safety of AF ablation.

Rationale for Catheter Ablation of AF

As outlined by the HRS Consensus Document on AF ablation, the primary indication for AF ablation is the presence of symptomatic AF

refractory, or intolerant, to at least one class 1 or 3 antiarrhythmic (AA) medication.¹ In specific situations, ablation may be considered as a first line treatment for AF; however this is not common practice.

The most common reason to pursue catheter ablation for AF is to reduce the patient’s AF burden. Therefore, ablation is performed to relieve symptoms and improve quality of life.^{1,3,5} As of today, it remains uncertain whether maintaining SR affects patient survival and, especially, stroke risk.^{6–13} However it appears that catheter ablation is more effective at maintaining SR as compared to AA therapy. Hopefully the CABANA study will provide insight into this and other important questions regarding the outcome of maintaining AF patients in SR by catheter ablation.

Typically, higher procedural success rates are reported in patients with paroxysmal AF and minimal structural heart disease.^{1,5} Yet published data also supports a role for catheter ablation in patients who were previously deemed unsuitable. Benefit from ablation has been reported in patients with heart failure^{14–17} and long-standing persistent AF.^{18,19} Success rates for catheter ablation of AF depend on various parameters. The type of AF (paroxysmal, persistent, or long-standing persistent), presence or absence of co-morbid conditions, duration of follow up as well as the definition of success are contributing parameters, some of which may need to be considered on an individual patient basis.¹ The HRS Consensus Document recommends that success be defined as freedom from symptomatic or asymptomatic AF, atrial tachycardia, or atrial flutter lasting 30 seconds or longer 12 months following AF ablation.¹ This should homogenise the often variable definition of success encountered in the past literature. From a clinical standpoint, a significant reduction of “AF

burden" associated with freedom from symptoms can be considered success. A three-month "blanking period" following ablation, where AA drug therapy can be continued, is recommended, as it is common to develop arrhythmia shortly following the procedure. Up to 60 % of patients who developed arrhythmia shortly after their procedure are free of AF during long-term follow up.

A desire to discontinue anticoagulation therapy is not an indication for ablation, as there is yet no consensus of long-term effects of catheter ablation with regard to risk of thromboembolic events.^{20,21} Even though stroke rate is low in these series, only a limited number of patients at high risk of stroke were followed free of anticoagulation for a significant period of time.

Current Techniques and Outcomes of Catheter Ablation for AF

It is now widely recognised that circumferential ablation of the PVs is the mainstay technique for most AF ablation procedures.¹ This reflects our understanding that ectopic beats originating in the PVs may be involved in the initiation of AF by acting as triggers. The primary procedural end point for this technique is to electrically isolate the PVs from the rest of the left atrium (LA).²² A series of point-by-point radiofrequency (RF) lesions are created to encircle the two left and two right PVs. Lesions may also be made between ipsilateral PVs, creating a lesion set resembling a figure of eight. Lesions are most frequently created using irrigated RF catheters. Localisation of the anatomical and electrical targets for ablation is achieved by the use of electroanatomic mapping systems. A CT or MRI scan performed before the procedure is used to determine the precise PV anatomy and can be merged with the electroanatomic map. In some cases, a pre-procedural echocardiogram may be needed to rule out the risk of thromboembolism. Ablation is carried out under conscious sedation or anaesthesia. It is becoming more common to perform AF procedures on patients fully anticoagulated with warfarin. Procedures are usually carried out on a short stay basis, with patients typically admitted overnight.

Electrical isolation of the PVs is usually confirmed by use of a circular mapping electrode (entrance block).²³ Pacing from within, or near, the PV can also be used to confirm electrical isolation (exit block).²³ Although recurrence of AF following PV isolation (PVI) is largely related to PV-LA reconnection, complete electrical isolation is not always necessary for therapeutic effect.²⁴ Similarly, even when complete bidirectional block is achieved, recurrence of AF can occur and therefore there may be a need to determine additional, perhaps substrate based, end points for PVI.²⁵

PVI can be achieved by means other than circumferential ablation of the PVs. Segmental PV ablation can be achieved by using a circular mapping catheter to guide placement of RF lesions. In some cases, only PVs demonstrating ectopic activity may be isolated. However, a large prospective, randomised control trial (RCT) concluded that circumferential isolation, with verification of conduction block, is the more effective procedure.²⁶ It is now recommended in the HRS Consensus Document that greatest success rates of PVI are achieved by circumferential ablation, and that this should be the goal of most PVI procedures.¹

Data from various types of clinical studies provide information concerning the success, outcome and safety of catheter ablation

for AF. A recent study describing the results of two meta-analyses concluded that ablation studies report greater success and safety in treating AF than studies involving AA drugs.²⁷ The authors included results from 63 studies, of any interventional study design, assessing the efficiency of catheter ablation for AF. Single procedure success rate of ablation off AA therapy was 57 % (95 % CI 50 %–64 %), the multiple procedure success rate off AA drugs was 71 % (95 % CI 65 %–77 %), and the multiple procedure success rate on AA or with unknown AA drug usage was 77 % (95 % CI 73 %–81 %). In comparison, the success rate for AA therapy was 52 % (95 % CI 47–57 %).²⁷

There are several available prospective RCTs comparing the relative success of catheter ablation and AA therapy in maintaining SR. A recent meta-analysis of a sample of the available RCTs directly compared the effect of catheter ablation to AA medication.²⁸ The authors reported that 76 % of patients treated with catheter ablation were free from AF, as compared to 18 % patients randomised to AA therapy.²⁸ This translates to a 3.7 fold greater chance of remaining in SR for those undergoing ablation.²⁸ The remaining RCTs confirm that ablation is more effective at maintaining SR than AA drugs.^{29,30} In these remaining trials, the success rates for ablation were reported at 89 % (compared to 23 % of AA drugs)³⁰ and 66 % (compared to 16 %).²⁹ Further analysis of the RCT conducted by Jais et al., revealed a significant improvement in quality of life and symptom control following ablation.³¹ This has also been reported previously by a separate group of authors in a non-randomised, prospective study.³²

A recent Cochrane review analysed the results 32 randomised control trials comparing catheter ablation to AA therapy for AF.³² The authors concluded that catheter ablation has a better effect in inhibiting recurrence of AF and maintaining SR as compared to AA drugs (RR 0.27; 95 % CI 0.18, 0.41). However, there were no differences in mortality (RR, 0.50, 95 % CI 0.04 to 5.65), fatal and non-fatal embolic complication (RR 1.01, 95 % CI 0.18 to 5.68) or death from thromboembolic events (RR 3.04, 95 % CI 0.13 to 73.43).³² Another recent systematic review included 108 studies comparing the outcome of catheter ablation for AF to antiarrhythmic therapy alone reached similar conclusions. Ablation was better at maintaining SR, however it is difficult to ascertain the effect it has on clinical prognosis as compared to AA drugs.³³ Several other available meta-analyses support these conclusions.^{34–36} Notably in one, the authors report a success rate of 77.8 % for catheter ablation as compared to 23.3 % for those in the control group, receiving AA drugs.³⁴

It is important to acknowledge that there is a trend to select relatively young patients with paroxysmal AF and limited co-morbidities for catheter ablation based treatment.³⁷ This bias is also observed in the selection process of most clinical trials. The potential benefit of catheter ablation excluded patients, especially those who fall under the broad category of "non-paroxysmal AF", has yet to be precisely defined. It is well recognised that the duration of continuous AF is an important predictor of the outcome of catheter ablation for AF1. In order to improve the outcome of catheter ablation in such patients, additional ablation techniques may be considered.^{1,24,25} There is considerable controversy surrounding the use of additional lesions sets during PVI. Additional ablation lines, such as roof lines or mitral isthmus lines may be used. However, their utility in persistent AF ablation has not been well quantified.¹ Some authors advocate targeting atrial areas displaying high degrees of fractionated atrial electrograms (known as Complex Fractionated Atrial Electrograms,

CFAEs).^{1,38} CFAEs are thought to represent areas of slow conduction and pivot points of re-entrant wavelets, which could act to sustain AF.³⁹ In one study, 40 patients in “chronic” AF underwent an ablation procedure involving identification and targeting of CFAEs.⁴⁰ Following circumferential PVI, which included roof line lesions, identification and ablation of CFAEs terminated AF in 73 % of patients.⁴⁰ Targeting CFAEs is not a universally accepted approach for persistent AF.¹ The lack of clear end-points, the inability to precisely determine which CFAEs are relevant to AF and the resultant extensive amount of ablation required limit the clinical use of CFAEs.¹

There is also a stepwise approach in whereby the procedure begins with PVI and continues using additional lesion sets until AF terminates.²⁶ However, this has been criticised by some as being a form of “atrial debulking”. A meta-analysis of studies comparing the outcome of these additional catheter ablation for non-paroxysmal AF patients reported similar procedural success rates for the various approaches, provided that circumferential isolation of the PVs, assessed by conduction block, was performed.¹⁹ It is hard to ascertain, currently, which procedure is optimal for patients with non-paroxysmal AF.

Additional techniques may also have a role in limiting AF recurrence following ablation. Studies examining the long-term benefit of AF ablation report significant recurrence rates following ablation.^{41–44} In the first of these trials, during mean follow-up of 28 ± 12 months, AF recurred in 23 patients (8.7 %). The actuarial recurrence rate of AF at five years was 25.5 %. AF recurrence was more likely in patients with hypertension and hyperlipidemia with a recurrence rate of 75 % if both of these risk factors were present. Similar findings have been reported in the other clinical trials. Overall, it appears that 20–40 % of patients require a second ablation procedure.⁴⁵ Recurrence following ablation usually requires additional procedures to restore SR, this may pose a significant risk and cost to patients. The main mechanism of recurrence appears to be reconnection of the PV-LA junction.⁴⁵ It is important to note that different techniques used to achieve PVI give rise to different rates of recurrence. Segmental PVI is thought to be less effective; one study reported that only 29 % of patients were free from AF at five years of follow up.³⁷ In a study using circumferential ablation, 47 % of patients were free from AF at 4.8 years of follow up. In both cases follow up was after a single procedure.^{41,43} These findings highlight the importance of creating more permanent lesions, a problem that emerging technologies may help ameliorate. It also appears that additional techniques, which help target substrates of AF, may yield more favourable outcomes for less suitable patient groups and those who experience recurrence.

Complications

Due to its demanding nature, catheter ablation of AF is associated with greater risk compared to other procedures carried out in the electrophysiology lab.¹ In 2005, an international survey of AF ablation procedures documented a 6 % risk of major complications. Major complications included cardiac tamponade (1.2 % incidence), peri-procedural stroke or TIA (0.94 % incidence) PV stenosis (1.3 % incidence), and death (0.05 % incidence).^{46,47} Greater experience with catheter ablation techniques is gradually decreasing the complication rate associated with the procedure. A recent update of the 2005 international survey reported a 4.5 % complication rate.⁴⁷ More evidence exists to support the idea that complication rates are gradually declining, with recent series reporting a 0.8 % rate of major complications, with no instances of death, stroke/TIA, atrial

esophageal fistula, or PV stenosis.⁴⁸ Importantly, a report from the International Survey of AF ablation from 162 centers reported details on 32 deaths, which occurred during, and/or following AF ablation procedures in 32,569 patients (0.1 %). Causes of death included tamponade in 8 patients (25 % of deaths), stroke in 5 (16 %), atriaesophageal fistula in 5 (16 %), and pneumonia in 2 (6 %).⁴⁷

Based on our review and knowledge of the literature as well as our clinical experience with AF ablation, we would estimate that the current incidence of major complications lies between 1 % and 4 %. The incidence of cardiac tamponade is 0.5 % to 1 %, stroke/TIA is 0.3 % to 1 %, vascular injury is 0.5 % to 1 %, pulmonary vein stenosis <0.5 %, and the risk for development of an atrial esophageal fistula and/or death is less than 0.1 %.

Areas of Uncertainty and New Techniques

There are areas regarding the ablation of AF that need to be better understood. For example, specific patient populations need to be better investigated. Elderly patients and patients with heart failure are currently underrepresented in the literature. One recent study reported no difference in AF control or complication rate in three age groups (<64 years old, 65–74 years old and >75 years old).⁴⁹ However, patients over the age of 75 were less likely to undergo repeated procedures and preferred to remain on AA drugs.⁴⁹ Various clinical trials have examined the role of catheter ablation of AF in congestive heart failure.^{14,16,17} The initial major study to address this issue examined the role of catheter ablation in 58 patients with heart failure who had an ejection fraction (EF) of less than 45 % compared to 58 controls.¹⁴ During a mean follow-up of 12 ± 7 months, 78 % of patients with heart failure and 84 % of controls remained in SR. The EF was observed to improved by 21 ± 13 %.¹⁴ Improvements were also seen in exercise capacity and quality of life.¹⁴ The Pulmonary Vein Antrum Isolation versus AV Node Ablation with Bi-Ventricular Pacing for Treatment of Atrial Fibrillation in Patients with Congestive Heart Failure (PABA-CHF) study compared the efficacy of AF ablation with AV node ablation and pacemaker implantation.¹⁶ This study demonstrated an overall superiority of PVI to AV-node ablation.¹⁶ A third case controlled series reported that the efficacy of AF ablation was similar in patients with and without LV systolic dysfunction and also reported an improvement in EF at six months follow-up.¹⁷ A recent meta-analysis reported that the single procedure efficacy of AF ablation was lower in patients with systolic dysfunction, but with repeat procedures a similar success rate could be achieved among patients with and without systolic dysfunction.⁵⁰ Overall, catheter ablation of AF is a reasonable in highly selected patients with heart failure.

Additionally, the interplay between the autonomic nervous system and AF is an area that has attracted attention recently (HRS). LA Ganglionated Plexi (GP) have been associated with triggering AF. Their ablation, concomitantly with PVI, has shown to decrease AF recurrence in one prospective RCT.⁵¹ Moreover, there is evidence to suggest ablation techniques involving Focal Impulse and Rotor Modulation (FIRM) may be of use in patients with non-paroxysmal AF.⁵² In this recent prospective RCT the detection of localised sources (electrical rotors and focal impulses) was common amongst patients with persistent AF. Ablation of such areas yielded greater freedom from AF (82.4 % versus 44.9 %; $p < 0.001$) than that observed in patients who underwent control procedures. Such studies highlight the need to better understand both the development of AF and how it is sustained, in order to achieve better results after catheter ablation.

Emerging Technologies

There has been a surge of new developments with regard to catheter ablation procedures for AF over the past years. Novel technologies aim to improve the safety and outcome of catheter ablation for AF, reduce procedure time and allow the procedure to be performed by less skilled operators.

It is well recognised that more permanent ablation lesions may provide an opportunity to better outcomes of catheter ablation for AF¹. Contact force is a major determinant of the size of the ablation lesion¹. To this end, RF catheters that provide the operator with feedback about the degree of force applied to the atrial wall are currently being developed.⁵³ These catheters were initially evaluated in Europe and released on a limited clinical basis. Currently there is no concrete data to establish a clear benefit of using such catheters. Despite the absence of definitive data, we feel the availability of ablation catheters which allow the operator to monitor feedback will represent a significant improvement in ablation technology which will translate to improved efficacy and lower complication rates.

Remote/automatic/robotic ablation tools are also being developed. Remote Navigation (RN) uses remotely controlled steerable sheaths to improve the manipulation of the catheters used during ablation.⁵⁴ Robotic Magnetic Navigation (RMN) systems employ two computer-controlled focused-field permanent magnets placed on either side of the patient by which the operator remotely controls the catheters.⁵⁴ Both these methods are being used clinically for the ablation of AF, however clinical data demonstrating better outcomes and safety is not yet available. MR imaging has also been used to guide AF ablation procedures in real time. Substantial progress has been made to incorporate this technique into clinical practice.⁵⁵

Recently, a cryoablation balloon system was approved for clinical use in the treatment of AF in the United States, although it has been available in Europe for many years. This system achieves PVI by freezing atrial tissue that comes into contact with a balloon that is cooled to -80 °C.^{56,57} The results of the United States based trial have been published in abstract form. Provisionally, the authors suggest a benefit as compared to ablation. A sample of 245 patients were randomised to either AA drugs or ablation, the procedure was successful in 70 % of patients. In comparison, the success rate for the AA therapy was 4 %.⁵³ A large number of trials have been published to evaluate the safety and efficacy of the cryoballoon ablation system in Europe. A large study published outcomes of 346 patients with predominantly paroxysmal, drug refractory AF. During a median follow-up of 12 months, SR was maintained (after one or more procedures) without the need for antiarrhythmic drug therapy in 74 % of patients with paroxysmal AF and in 42 % of patients with persistent AF.^{56,57} Another balloon based PV ablation system uses

laser energy produced by a diode laser to create atrial lesions. A circumferential decapolar PV ablation catheter, which uses phased RF energy to create lesions, is also being evaluated for PVI. There is little data to suggest a role for these systems, although clinical trials are underway in order to do so.^{55,56} Finally, a hybrid thoracoscopic and transvenous catheter approach has been investigated in a recent prospective single centre study. The authors report a single procedure success rate of 86 % for the 26 patients who enrolled. Although the study has limitations, this is the first attempt to integrate surgical and percutaneous approaches for AF ablation. Moreover, the results provide further support that PVI is the cornerstone procedure by which to ablate AF, especially for patients with paroxysmal AF.⁵⁸

Conclusion

Catheter ablation is now an important, well-established treatment option for patients with AF. We know, through a considerable body of evidence, that catheter ablation is more successful at maintaining SR than AA drugs. Additionally, catheter ablation provides better symptomatic control for patients, and therefore improves their quality of life. Currently, it appears that the most effective technique for catheter ablation of AF is the circumferential isolation PVs. These conclusions are particularly true for patients with paroxysmal AF who have relatively little co-morbid disease and structurally normal hearts. However, ablation is becoming an option for an increasingly diverse population of patients. In these patients, it may be necessary for additional techniques to be added to the ablation procedure. However, it is currently not known which procedure is optimal for cases of non-paroxysmal AF. In some cases, ablation may even constitute a first line therapy; however, this is rare practice. It is important to appreciate that ablation for AF does not guarantee SR. The recurrence rate is high, and many patients will require more than one procedure. New technologies and emerging techniques will hopefully improve the success rates of catheter ablation for less suitable patient groups, whilst also help limit recurrence.

Currently, the impact of catheter ablation for AF has a long-term clinical outcome, especially in terms of survival and has not been precisely quantified. In patients who are symptomatic, it is preferable to consider catheter ablation as a treatment for AF early on. This may also help prevent the atrial remodeling that occurs during AF, and limit disease progression. However, in patients with paroxysmal AF who are not symptomatic and can be maintained in SR with AA drugs, postponing ablation may be the preferable option. This reflects the fact that catheter ablation is not a risk-free procedure; important complications need to be considered by the patient and physician. With time ablation procedures are becoming safer and more effective, and are now most common electrophysiology procedures today. This is a remarkable achievement for a procedure that is no more than 20 years old. ■

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