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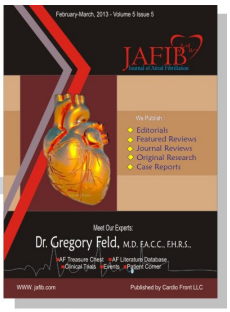

Catheter Ablation of Long Standing Persistent Atrial Fibrillation: Lessons Learned

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Abstract

Atrial fibrillation has evolved from being a novel unproven procedure to being an important treatment option for patients with symptomatic atrial fibrillation. Atrial fibrillation ablation is an appropriate treatment option for patients with symptomatic atrial fibrillation, particularly if they have failed one or more trials of antiarrhythmic drug therapy. While much has been learned about the optimal technique and outcomes for catheter ablation of paroxysmal atrial fibrillation; catheter ablation of atrial fibrillation in patients with long standing persistent atrial fibrillation remains in its infancy. The following objectives would be accomplished in this review article.

First, we will review the various ablation strategies, which have been employed and proposed for ablation of long standing persistent atrial fibrillation. Second, the methodology, results and outcomes of the major studies were reviewed in detail, which have reported outcomes of ablation in this patient population. And finally, some conclusions were drawn regarding where we stand and where the knowledge gaps remain as we seek to improve ablation outcomes in this population of AF patients.

Introduction

Over the past decade catheter ablation of atrial fibrillation (AF) has evolved from being a novel unproven procedure to being an important treatment option for patients with symptomatic AF. According to the 2012 HRS/ECAS/ECHRA Consensus document on catheter ablation of AF, AF ablation is an appropriate treatment option for patients with symptomatic AF, particularly if they have failed one or more trials of antiarrhythmic drug therapy.[1-4] While much has been learned about the optimal technique and outcomes for catheter ablation of paroxysmal AF; catheter ablation of AF in patients with long standing persistent AF (LSPAF) remains in its infancy. Very few studies have been published which report the technique and outcomes of catheter ablation in patients who have LSPAF, defined as continuous AF for 12 months or longer

This review article seeks to accomplish three objectives. First we will review the various ablation strategies, which have been employed and proposed for ablation of (LSPAF). Second, the methodology, results and outcomes of the major studies were reviewed in detail, which have reported outcomes of ablation in this patient population. And finally, some conclusions were drawn regarding where we stand and where the knowledge gaps remain as we seek to improve ablation

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outcomes in this population of AF patients.

Catheter Ablation Strategies for Treatment of Long Standing Persistent Atrial Fibrillation

In catheter ablation of LSPAF, pulmonary vein isolation (PVI) can be done alone or in combination with other methods like modification of the left atrium or pre-ablative preparation. There are four ablation strategies that incorporate these concepts and have been identified in ablation of LSPAF

The first strategy is PVI alone. In the recent HRS/EHRA/ECAS AF Ablation Consensus Document, it is notable that electrical isolation of the pulmonary veins (PV) is identified as the "cornerstone" for most AF ablation procedures.[5] The importance of the PVs as the most common source for AF triggers was initially reported by Haissaguerre and colleagues in 1998.[6] Since this landmark publication, other investigators throughout the world have confirmed these findings. Thus, it is now widely believed that the most important component of AF ablation today is achieving permanent electrical isolation of the PVs. This is most commonly accomplished with a wide area circumferential approach with electrical isolation of the PVs confirmed with a multipolar circular electrode mapping catheter. Not only does this approach seek to achieve electrical isolation of the PVs, thereby preventing rapid firing of the PVs from triggering AF, but the ablation trajectory is directed through many of the autonomic ganglia. Proponents of the PV isolation alone argue that until electrical isolation of the PVs is achieved, it is inappropriate to ablate other areas of the atrium, an approach they consider in a negative light as "atrial debulking".

A second approach, which has been developed for ablation of LSPAF, is the "stepwise approach" developed by Michel Haissaguerre and colleagues.[7] The stepwise approach combines in a stepwise and sequential fashion PVI, linear ablation at the roof and mitral isthmus, and left and right atrial CFAE ablation. The endpoint of ablation for the sequential approach is termination of AF. Observing a progressive lengthening of the AF cycle length as each step of the ablation strategy is completed can assess the progress of ablation. AF either terminates directly to sinus rhythm, or more commonly converts to atrial tachycardia, which can then be mapped and ablated. The linear ablations in the left atrium have anti-fibrillatory effects in helping restore sinus rhythm.

A third strategy, initially described by Steinberg et al is based on the concept that the preablative use of antiarrhythmic drugs (AAD) and cardioversion in patients with persistent AF with restoration of sinus rhythm would lead to reverse atrial remodeling thereby allowing conventional PV isolation to achieve a far higher long term efficacy than it otherwise would.[8] In their initial report they administered dofetilide before PVI isolation and 1-3months post ablation. The ablation strategy they employed was standard wide area circumferential ablation to achieve pulmonary vein isolation. More recently Haissaguerre and colleagues have confirmed their findings. In this recent study they compared two ablation strategies in patients with persistent and long standing persistent AF.[9] One group was brought to the EP laboratory in atrial fibrillation whereas in the other group sinus rhythm was restored prior to ablation using antiarrhythmic drug therapy and cardioversion.

A fourth strategy that has been recommended for ablation of LSPAF is targeting complex fractionated atrial electrograms (CFAE) alone. Nademanee and colleagues described this technique as detailed mapping of the right and left atria demonstrated by CFAE electrograms. In their study, CFAE electrograms were defined as: 1) atrial electrograms that have fractionated electrograms composed of two deflections or more, and/or perturbation of the baseline with continuous deflection of a prolonged activation complex over a 10 second recording period; 2) atrial electrograms with a very short cycle length (< 120 ms) averaged over a 10 second recording period.[9] It is notable that this technique, when applied in its purest form, does not involve electrical isolation of the PVs.

A Review of Major Studies in this Field

We performed an extensive literature search of electronic databases including PubMed, EMBASE and the Cochrane Library. Although we found a large number of papers that have reported outcomes of mixed populations of AF patients, which may or may not have included a small subset of patients with LSPAF, we identified very few manuscripts

that have included only patients with LSPAF. In order to broaden our review of the literature we have decided to also review papers which report outcomes of AF ablation of patients with LSPAF as well as other types of AF provided the following criteria are met: 1) the number of patients in the study who had LSPAF should be >50 and 2) the mean follow up after the first ablation should be approximately one year or longer.

Five studies satisfied our criteria for a detailed review. Among these five studies, 2 reported the outcomes of CFAE alone, 2 reported the outcomes of PVI or antrum ablation with CFAE while 1 reported the outcomes of stepwise approach. Each study will be summarized based on the year of publication with the oldest paper first and most recent paper last.

The first study was published by Oral et al in 2007 in the Circulation. In this study 100 patients had radiofrequency catheter ablation for atrial fibrillation guided by CFAE. AF was present for about 5 + 6 years before ablation. CFAE were defined as electrograms with cycle length <120ms or shorter than in the coronary sinus or that were fractionated or displayed continuous electric activity.[10-12] PV were mapped and areas that displayed CFAE were ablated with endpoint of elimination of CFAE not PVI. After ablation of CFAE in the left atrium, CFAE within the coronary sinus were ablated. The goal of ablation was AF termination or elimination of all identified CFAE. AF terminated with ablation in 16 patients (16%) while additional 40 patients terminated after infusion of ibutilide. The mean procedure and fluoroscopy times were 206 + 43 and 51 + 16 minutes respectively. They found that during 14 + 7 months of follow up after a single procedure, 33% patients were in sinus rhythm without antiarrhythmic drugs. After repeat ablation and a mean follow-up of 13 + 7 months, 57 patients (57%) were in sinus rhythm in the absence of antiarrhythmic drug therapy. Complications reported in the study included pericardial tamponade in 2 patients, which was treated with percardiocentesis, and transient ischemic attack in one patient, which resolved within hours after the procedure.[11]

The second study was published by Elayi et al. in Heart Rhythm journal in 2008. The outcomes of 3 ablation strategies were compared in 144 patients with longstanding persistent atrial fibrillation (median AF duration 28 months).[12] Group 1 underwent circumferential pulmonary vein ablation. Group 2 also underwent circumferential PV isolation plus antrum ablation. The antrum included the entire posterior wall and extended anterior to the right PVs along the left septum. Group 3 underwent circumferential PV isolation with ablation of the antrum as well as ablation of CFAEs in both atria. After mean follow-up of 16 months, 11% of 47 patients in Group 1, 40% of 48 patients in Group 2 and 61% of 49 patients in Group 3 remained in sinus rhythm after one procedure and with no antiarrhythmic drugs. Subsequent maintenance of sinus rhythm was increased to 28% (group 1), 83% (group 2), and 94% (group 3) after 2 procedures and with antiarrhythmic drugs. AF conversion to atrial tachycardia occurred more often for group 3 (70%), less often for group 2 (38%) and rarely for in group 1 (11%). Group 3 had a statistically longer fluoroscopy time (94 + 27 min) than group 2 (76.9 + 21min) or group 1 (50.1 + 21 min), (P= 0.016). Procedure times were 131 + 82 min (group 1), 183 + 91 min (group 2) and 239 + 102 min (group 3). They concluded that hybrid atrial fibrillation ablation strategy including antrum isolation and CFAE ablation had the highest likelihood of maintaining sinus rhythm in patient with LSPAF. Complications reported in the study included pericardial effusions in 2 patients and asymptomatic PV stenosis in 2 patients.

A third study was published by Oral et al. in Circulation: Arrhythmia and Electrophysiology in 2008.[13] They studied 85 patients with LSPAF where the radiofrequency ablation (RFA) was directed at CFAE in the LA and coronary sinus until AF was terminated (19 patients) or all identified LA CFAEs were eliminated. They ablated only CFAE with no PVI. The end point of CFAE ablation in the RA was conversion of AF to sinus rhythm or atrial flutter or ablation of all identified CFAEs. Single procedure success rate off drugs after LA RFA for AF was 22% (19 patients). Sixty-six patients who remained in AF were randomly assigned to cardioversion and no further RFA (33 patients) or to RFA of the RA CFAEs (33 patients). After 16 + 7 months of follow up, 17 patients (52%) were in sinus rhythm without antiarrhythmics, 8 patients (24%) in persistent

AF, 5 patients (15%) in paroxysmal AF, 3 patients (9%) in atrial flutter in the group with no further RFA. While in the group that had RA RFA, 19 patients (58%) were in SR without antiarrthymics, 8 patients (24%) in persistent AF, 3 patients (9%) in paroxysmal AF, 3 patients (9%) in atrial flutter after 16 + 7 months follow up.[13] They concluded that after RFA of CFAE in the LA and coronary sinus, ablation of CFAE in the RA provides little or no increment in efficacy among patients with LSPAF. The mean procedure and fluoroscopy times for the LA RFA were 198 + 74 minutes and 57 + 21 minutes, respectively while for the RA RFA mean procedure and fluoroscopy times were 25.2 + 13.6 and 6.9 + 4.2 minutes, respectively. One complication was reported in the study, which was pericarditis after left atrial ablation that did not require any intervention.

A fourth study by O'Neill et al was published in European Heart Journal in 2009 which prospectively studied 153 consecutive patients who underwent catheter ablation of AF (median duration 12 months) using a stepwise approach with a desired end point of atrial fibrillation termination, found that AF terminated in 130 (85%) of the patients with ablation alone. [14] Repeat ablation was performed for patient with recurrent AF or atrial tachycardia after 1 month blanking period. The median duration of the sustained AF was 12 months with a minimum follow-up of 12 months after the ablation. Seventy-nine patients required repeat ablation procedures. At a median of 34 months of follow-up, 124/130 patients (95%) in the AF termination group were in stable sinus rhythm after the last procedure while it was 12/23 patients (52%) in the AF Non-Termination group. The single procedure success rate was 48%, which improved to 74% after multiple procedures. The procedure time for RFA was 88 + 27 minutes. Complications reported were tamponade in 2 patients, femoral hematomas in 2 patients and reversible phrenic nerve injuries in 2 patients. They concluded that termination of persistent AF by catheter ablation was associated with a better long-term clinical outcome than when AF was not terminated.

The fifth study by Tilz et al was reported in the Journal of Cardiovascular Electrophysiology in 2010. They studied the outcomes of 205 consecutive patients who underwent catheter ablation for LSPAF.[15] The median duration of continuous AF was 36 months (range 22 to 60). They performed circumferential pulmonary vein isolation (CPVI) in 205 (60.5%) patients while additional CFAE ablation, left linear lesion ablation or SVC isolation was performed in others if direct-current cardioversion failed after CPVI. The goal was conversion to sinus rhythm or atrial tachycardia with subsequent ablation. After a mean follow-up of 19 + 11 months, 67 of 199 patients remained in sinus rhythm. After a mean of 1.7 + 0.8 procedures, 67.8% of the patients were in sinus rhythm. The success rate following a single CPVI as first line was 33%, which improved to 68% in nearly half of the patients after multiple procedures for sinus rhythm (SR). The major complication rate found in the study was 4%, which included ischemic stroke (0.6%), transient ischemic attack (0.3%), groin hematomas (2.4%), aspiration pneumonia (0.3%), pneumothorax (0.3%) and pulmonary edema (0.3%). Mean procedure and fluoroscopic times were 210 + 72 and 28 + 13 minutes, respectively. They concluded that CPVI alone is sufficient to restore sinus rhythm in 43.2% of patients with LSPAF with possibility of needing multiple procedures in those who could not achieve SR.

The sixth study by Takahashi et al was reported in Circulation: Arrhythmia and Electrophysiology in 2010. They studied 93 patients who underwent left atrial ablation for persistent atrial fibrillation. The median duration of AF was 1 year. Left atrial ablation consisted of pulmonary vein isolation, linear ablation, and electrogram-based ablation. After the first procedure, 35 patients (38%) remained free from tachyarrhythmias, 27 patients (29%) had atrial tachycardia, and 31 patients (33%) had AF. The 31 patients who AF recurred, electrogram-based ablation were performed in the right atrium in 26 patients. During the 2 year follow up and after a median of 2 procedures, 82% of the patients were free from any tachyarrhythmias. The complication rate was 2% (2 patients), which included a stroke and a pericardial effusion. They concluded that persistent AF with shorter duration was more likely to be free from AF by LA ablation.[16]

Lessons Learned

For many years we have employed a strategy of trying to restore sinus rhythm prior to performing an AF ablation procedure in patients with continuous AF. This often requires use of amiodarone,

dofetilide, and cardioversion initiated one or more months prior to the procedure. As a result of this approach almost all of our patients present in sinus rhythm, which some people may consider as selection bias. But, in our mind this both lowers risk of stroke and improves efficacy. During a first procedure we perform wide area circumferential PV isolation. If AF recurs following the blanking period patients are offered a repeat ablation procedure. If PV reconduction is observed we will reisolate the PVs. We also commonly perform a roof and floor line to create a posterior wall "box" lesion. We only employ a CAFÉ based approach if the PVs show no evidence of reconnection. With this approach we have achieved results comparable to those published in the literature, but with a lower risk of complications. We also feel that our approach results in less destruction of healthy atrial tissue.

Conclusions

This review on the technique and outcomes of AF ablation in patients with LSPAF suggests that catheter ablation of LSPAF remains in its infancy. Although a number of different ablation strategies have been developed, little data exists to determine the optimal approach. It is striking how limited the literature is which has focused on the technique and outcomes of catheter ablation of LSPAF. Those studies which have been published have important limitations. First, these studies were not large adequately powered studies which were performed in a prospective blinded fashion. Secondly, the duration of follow-up is relatively short. We are well aware of the important issue of late recurrences of AF more than one year following AF ablation. And third, many studies do not report the single procedure success rate off of antiarrhythmic drugs, as recommended by the 2012 HRS Consensus Document on AF Ablation.

Recent techniques like clinical mapping of electrical rotors and focal impulse in humans have been developed to improve the efficacy of ablation of persistent AF.[17] We are hopeful that in the years ahead researchers in the field will keep focusing on the important topic of catheter ablation of long standing persistent AF.

Disclosures

No disclosures relevant to this article were made by the authors.

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