ATRIAL FIBRILLATION

RESEARCH ARTICLE

Long-term Follow-up of FIRM-guided Ablation of Atrial Fibrillation: A Single-center Experience

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ABSTRACT. Radiofrequency catheter ablation (RFCA) of atrial fibrillation (AF) guided by focal impulse and rotor modulation (FIRM) has been shown to result in short-term clinical freedom from AF. However, there are limited long-term outcome data available, especially in the more persistent and repeat ablation population. Therefore, we report our long-term results from a single site center performing FIRM-guided RFCA of AF. A total of 80 patients were evaluated after undergoing FIRM-guided AF RFCA. The first analysis included an in-depth assessment of rotor characteristics and 2-year procedural outcomes in a testing period (phase I) in the first 36 patients. A second analysis assessed the procedural outcomes in 80 consecutive patients comprising those in phase I and the following 44 patients in a validation phase II. All patients underwent FIRM-guided RFCA in addition to pulmonary vein (PV) antral isolation and additional atrial tachycardia (AT) atrial flutter (AFL) ablation as needed. The endpoint of FIRM mapping/ablation was the elimination of all rotors and focal activation patterns in both atria. Follow-up included assessment of frequent 12-lead electrocardiograms, stored pulse rates recorded twice daily, and 30-day loop recorders. Rotors were identified and ablated in all 80 patients. In phase I, 83% (31/36 patients) had structural heart disease (SHD). Types of AF were paroxysmal in 36% (13/36) of patients, persistent in 53% (19/36) of patients, and longstanding persistent in 11% (4/36) of patients. Fifty percent (18/36) patients had prior ablations at 1.3 ± 0.8 (range 1–4) years. AF termination during FIRM RFCA occurred in 39% (14/36) patients (64% (P AF), 36% persistent AF) and in 18% of all mapped episodes (25/138 rotor/FA). Overall single procedure 2-year freedom from AF/AFL rate in phase I was 81% (29/36) (83% in patients at first ablation, 78% in patients with prior ablation). Success rates off and on medications were 85% and 92% PAF, 58% and 79% persistent AF, 25% and 50% longstanding persistent AF, respectively. In the 39% patients with procedural AF termination, the 2-year success rate was high at 86% (12/14). Combining patients in phases I and II, with similar demographics, freedom from AF/AFL was 75% at 16 ± 7 months. Predictors of recurrence after FIRM-guided ablation were persistent/longstanding AF, larger left atrium (LA) size, a longer AF history, and termination of AF/AFL by either cardioversion or LA linear lines. FIRM-guided AF RFCA demonstrated a promising long-term success rate in a patient population with SHD and previous ablation when performed in addition to PV antral isolation (PVI) and AT/AFL ablation. The high long-term success rates were similar for both first and repeat AF ablation patients. The results of this study strongly warrant randomized control trials.

KEYWORDS. atrial fibrillation, catheter ablation, focal impulse and rotor modulation (FIRM), rotors.

Introduction

Radiofrequency catheter ablation (RFCA) of atrial fibrillation (AF) has historically been associated with rather poor long-term success and high recurrence. For instance, long-term single procedure success of traditional ablation is approximately 50-60% for paroxysmal AF (PAF), and even
lower for non-paroxysmal forms of AF. Moreover, post AF ablation patients have a high 90 day recurrence rate at approximately 50% in a PAF population and as high as 58% in a mixed paroxysmal/persistent AF population. Triggered activity within the left atrial pulmonary veins (PVs) and antrum has been shown as an AF initiator in patients with PAF. As a result, elimination of conduction within those structures has been the primary goal of AF ablation. Recently, however, electrical mapping with the use of a 64-electrode basket catheter has demonstrated the presence of bi-atrial rotors and focal sources in AF, many times arising from outside of the PV and antrum. The rotor core is the primary driving mechanism for AF sustenance. Studies have suggested that ablative targeting of the rotor core and focal sources either alone or in combination with traditional ablation approaches can significantly reduce AF burden compared with traditional ablation approaches alone; however, many of those studies report only short-term outcomes and results. In addition, the studies lack the wider spectrum of AF patients undergoing RFCA in many community clinical centers such as the redo ablation population and the more persistent types of AF. Therefore, the aim of this single-center observational experience was to assess the long-term 2-year clinical outcomes associated with FIRM-guided ablation in patients with both paroxysmal and more persistent forms of AF as well as in the repeat ablation AF population.

Methods

Patient enrollment

Phase I reports detailed analyses in 36 consecutive patients undergoing FIRM-guided AF mapping and ablation in the 15-month period from January 2013 to March 2014. Paroxysmal, persistent, and longstanding persistent AF patients were all included in this evaluation and were referred for catheter ablation of drug refractory AF. All patients met the standard indications for AF ablation. Phase II reports follow-up information in the next consecutive 44 patients undergoing the same FIRM mapping and ablation protocol from March 2014 to January 2015. All patients provided written informed consent.

Procedural details

Procedures were performed more than five half-lives after discontinuing antiarrhythmic medications except for amiodarone, which was stopped 12 weeks before ablation. A multipolar catheter was placed in the coronary sinus via right jugular vein access. Using the right femoral vein approach, a 64-pole basket catheter was advanced to the right then left atrium via a long intravascular 8.5F sheath. An irrigated ablation catheter (ThermoCool, Biosense-Webster, Diamond Bar, CA) was advanced to the right atrium (RA) and left atrium (LA) via right femoral vein access. An intracardiac echocardiography (ICE) catheter (Soundstar, Biosense-Webster, Diamond Bar, CA) and a 6F Quadripolar catheter were positioned in the right atrium using the left femoral vein. Fluoroscopy and intracardiac echocardiography were used to achieve optimal contact with the atrial endocardium. Heparin was administered by infusion before basket placement to maintain activated clotting time (ACT) > 350 s. If AF was not present upon arrival at the laboratory, AF was induced by rapid atrial pacing with isoproterenol infusion if needed. Sustained AF was then defined as > 10 min in duration. AF recordings were obtained from either the Constellation™ (Boston Scientific Corp., Natick, MA) or the FIRMMap™ (Topera Inc., Menlo Park, CA) 64-pole basket catheter (Figure 1). Unipolar electrograms were filtered at 0.05–500 Hz and exported digitally from the electrophysiological recorder (Prucka, GE Medical Systems, Milwaukee, WI) for analysis and the creation of rotor maps using RhythmView™ (Topera Inc., Menlo Park, CA).

AF mapping and definition of stable rotors

The FIRM-guided ablation workflow is illustrated in Figure 2. In short, basket catheters were placed successively in each atrium to record AF electrograms after RA and LA activation maps were created by a three-dimensional (3D) mapping system. Basket catheter size was determined by measurements of the LA performed by both ICE and CT scan images. Constellation™ baskets (sizes 48 and 60 mm) were used for rotor mapping in the first 17 patients. Rotor mapping was performed in the remaining 63 patients utilizing FIRMMap™ baskets (sizes 50, 60, or 70 mm). Electrograms were then exported for analysis by the RhythmView™ workstation. Using a

Figure 1: Two different 64-pole basket catheters were utilized during the study. The Constellation™ catheter (left) had an asymmetrical distribution of electrodes (more electrodes distally) with smaller interelectrode spacing while the FIRMMap™ catheter (right) had more evenly spaced electrodes with larger interelectrode distance.
previously described computational approach, the software creates an activation trail that can identify AF rotors and focal activations within the atria^{10–12} (Figure 3). The resulting AF maps are then projected onto two-dimensional grids aligned to atrial anatomy. FIRM ablation of rotors

RFCA commenced at rotors/ectopic focus identified from FIRM maps of AF. Using irrigated catheters at 25–40 W, radiofrequency (RF) energy was applied to the basket grid coordinates corresponding with the center of rotor rotation (typically areas of ~2 cm²), as identified from electrode positions on electroanatomic 3D shells. Ablation was performed typically for 5–6 min per location whether or not AF had terminated. Additional RA and LA sites of ablation were targeted until all rotors were eliminated, confirmed by repeat AF FIRM maps. Conventional ablation was then performed after FIRM-guided rotor ablation was completed, which consisted of wide-area LA antral isolation, as verified using a circular catheter (Lasso™, Biosense-Webster, Diamond Bar, CA). Additional ablation was performed, if indicated, which included a LA roof line and/or ablation of observed clinically relevant atrial tachycardias or flutters. If AF/AFL persisted after completion of the ablation protocol, cardioversion was performed to restore sinus rhythm.

Follow-up clinical management and endpoints

Patients were followed as per standard of care and consistent with societal guidelines. In the follow-up period were 12-lead electrocardiograms obtained at 3, 6, 12, 18, 24 months, and every 6 months thereafter. Stored pulse rates were recorded, twice daily if available; also included were 30-day loop recordings after 3 months, and anytime pulse irregularity or symptoms were noted or implanted device data, if available. Arrhythmia recurrence was defined as symptomatic or asymptomatic episode of AF >30 s after a 3-month blanking period. The primary effectiveness endpoint was sinus rhythm, defined as no arrhythmia for >30 s on intermittent monitoring. Secondary effectiveness endpoints included outcomes in patients undergoing a first ablation and outcomes in patients with paroxysmal, persistent, and longstanding AF at follow-up.

Statistical analysis

Continuous data are represented as mean ± 1 standard deviation (SD). The Fisher exact test or a binomial probability distribution was applied to categorical variables, as appropriate. A p-value of <0.05 was considered statistically significant.

Results

Characteristics and procedural data

Patient characteristics in both phases are summarized in Table 1. There was a very high incidence of structural heart disease and LA enlargement in all 80 patients as noted. Table 2 summarizes detailed number and distribution of rotors in both atria and the percentage of AF terminations.
during RFCA in the first 36 patients in phase I. AF rotors were identified in all patients. As demonstrated, 68% (63/92) of LA rotors were identified outside the LA PV antrum and posterior wall. Procedural AF terminations occurred in 14/36 patients (39%) with 64% in paroxysmal, 36% in persistent, and 0% in longstanding persistent AF patients. The number of patients with AF termination was the same for the repeat as well as the first ablation populations 7/18 (39%). During RFCA, conversion of AF to AFL/AT occurred in 25% (9/36) patients with an incidence of 7% per targeted source (9/138 sources: four in the RA, five in the LA). Focal activation patterns were 75% LA in origin and present in 11% (4/36) of patients with an incidence of 4% (5/138 mapped episodes).

Combining phases I and II (n = 80), total fluoroscopy and procedural times were 36 ± 20 min and 280 ± 60 min respectively. Atrial flutters, either spontaneous or inducible, were ablated in 49% (39/80) patients (RA in 22 and LA in 26 patients). AT/AVnRT was ablated in eight patients (4 RA, 4 LA). Total RFCA time including conventional ablation was 76 ± 25 min. Five complications were noted including a moderate size left groin hematoma and two moderate size pericardial effusions; all were resolved with conservative treatment. Two episodes of pulmonary edema developed postoperatively requiring aggressive diuresis.

Clinical outcomes

Table 3 shows that the overall single FIRM-guided procedure success in phase I was 81% (29/36) for all patients and 83% (15/18) in patients undergoing their first FIRM-guided ablation procedure. The differences in the success rates of various types of AF in patients both on and off antiarrhythmic medications are also listed. Figure 4 shows 2-year freedom from AF/AFL based on type of AF and initial versus repeat procedure for each of the first 36 patients in phase I on antiarrhythmic medications. The 2-year freedom from AF/AFL in patients that AF terminated during RFCA was 86% (12/14: 6 repeat, 6 first ablation) off medications. Taking a selected difficult subset of repeat ablation patients with more than two previous ablations, 80% (8/10) remained in sinus rhythm at 2 years off medications. Table 4 shows the ablation outcomes in phase I (n = 36 patients) and combined phases (n = 79/80 patients: follow-up not available in one patient) for each type of AF and for repeat and first ablation patients. Examining phase II (n = 80), one patient was lost to follow-up. In the remaining 79, 20 patients had recurrence. Of these recurrences (n = 20/79), 45% (9/20) were
repeat ablations, 90% (18/20) had persistent/longstanding persistent AF, and 85% were male (17/20). In addition, the patients had an AF history of 9 ± 6 years with a persistent AF duration before the ablation of 8 ± 4 months. Their LA size was 59 ± 6 mm.

Examining recurrent arrhythmias in phase II from a procedural standpoint, atypical AFL accounted for 80% (16/20) and 20% recurred with AF. Additional LA linear lines after FIRM and PVI were required in 60% (12/20) of those patients. At the end of the procedure, 70% (14/20) of patients required cardioversion of either AF (50%) or AFL (50%).

On follow-up, one patient died due to cardiac failure at 6 months. There were no procedure-related deaths.

Discussion

In this large single-center report of FIRM-guided ablation, all patients exhibited stable rotors and focal sources. Sources lay in right and left atrium in patients with PAF as well as persistent AF and with de novo AF as well as recurrent AF despite unsuccessful ablation. Single FIRM-guided ablation procedural freedom from AF and AFL was 75% at 16 ± 7 months in this population, of whom 75% had persistent or longstanding persistent AF, and was maintained for nearly 2 years in the subset of patients in phase I. The results were similar in patients with no prior ablation procedure or prior non-FIRM ablation procedures. The data compare favorably with prior published data from conventional ablation, and strongly motivate randomized controlled trials.

Rotor and focal activation characteristics

Confirmation of the existence of localized rotors and focal atrial sources in human AF has only recently been reported.5,6 However, there is a growing body of literature that supports the importance of rotors in sustaining AF.7–12 Rotors and focal sources have been characterized in both PAF and more persistent AF types.8,10,11 Our independent single site FIRM mapping experience has confirmed the presence of both rotors and focal activations in all types of AF: paroxysmal, persistent, and longstanding persistent. In fact, the location and distribution of rotors identified in this study are consistent with those identified with previously published results of FIRM-guided ablation.8,10,11 Similar to both the CONFIRM trial10 and Multicenter FIRM registry11 data, a large percentage of LA rotors in this study were identified outside the PVs and the posterior wall. In addition, the incidence of RA rotors between the three studies was comparable. There were a few notable differences seen in our investigation. Firstly, a larger number of rotors per patient was present with an average of 3.8 in our study compared to 2.3 in the other two trials.8,11 Secondly, a much lower incidence of focal sources were identified (~4%) compared with the CONFIRM trial at 30%.8 Finally, the presence of RA rotors was seen in a higher percentage in our patients (75% versus 50% in the registry11). The differences may be due to multiple factors including differences in the interpretative skills between centers, improvement in mapping software, different patient populations (high CABG, OSA, CHF incidence), and the use of two basket mapping catheters (FIRMap™ and Constellation™ catheters) compared with the Constellation™ catheter alone.8,10,11

AF termination

Rotor ablation directed at the core has been shown to acutely terminate AF9 and several mechanisms have recently been proposed.16 In the CONFIRM trial, AF terminated during RFCA in 56% of patients compared with 39% of patients in our study; however results from both the CONFIRM10 and PRECISE17 trials show that elimination of all AF rotors/sources confirmed by repeat FIRM maps can be an effective endpoint. Our data

Table 3: Two-year clinical freedom from AF and AFL in phase I (first 36 patients) on and off previously ineffective antiarrhythmic medications

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>% Sinus rhythm on AA</th>
<th>% Sinus rhythm off AA</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 36 patients</td>
<td>81 (29/36)</td>
<td>64* (23/36)</td>
</tr>
<tr>
<td>First ablation</td>
<td>83 (15/18)</td>
<td>67* (12/18)</td>
</tr>
<tr>
<td>Re-do ablation</td>
<td>78 (14/18)</td>
<td>62 (11/18)</td>
</tr>
<tr>
<td>Paroxysmal AF (n = 13)</td>
<td>92 (12/13)</td>
<td>85 (11/13)</td>
</tr>
<tr>
<td>Persistent AF (n = 19)</td>
<td>79 (15/19)</td>
<td>58* (11/19)</td>
</tr>
<tr>
<td>Longstanding persistent AF (n = 4)</td>
<td>50 (2/4)</td>
<td>25 (1/4)</td>
</tr>
</tbody>
</table>

*Three patients without AF recurrence decided to stay on medications.

AA: antiarrhythmic medications; AF: atrial fibrillation.

Figure 4: Flow diagram of 2-year freedom from atrial fibrillation (AF) and atrial flutter (AFL) rates of phase I (first 36 patients) depicting the breakdown of both the first and repeat ablation results for each type of AF.
confirm this premise, as the overall incidence of AF termination during RFCA was low (23%) and yet the total patient 2-year ablation success was 75%. Interestingly, however, our data do suggest that when AF termination did occur in a patient, the long-term freedom from AF off antiarrhythmic agents was high (86%).

FIRM-guided ablation outcomes compared with previous published results

Previous studies have shown that FIRM-guided RFCA of AF improves AF freedom compared with conventional ablation alone. The clinical outcomes reported in this investigation are similar to one year previously published results of FIRM-guided ablation. The 81% overall single FIRM-guided procedure success in our first 36 patients (phase I) reported in this study is consistent with the results of the CONFIRM trial as well as the multicenter registry (82.4% and 80.5%, respectively). In addition, our single FIRM-guided procedure 2-year freedom from AF/AFL for the 80 patients (phase I and II combined) undergoing first ablation results are similar to the 3-year results after FIRM-guided ablation and PV1 at 77% versus 75%, respectively. Thus, our data, comprising acute AF termination by localized rotor ablation alone in many patients coupled with high single-procedure long-term arrhythmia freedom, further validate the conclusions from previous studies of the important mechanistic role of rotors in sustaining AF. Conversely, single procedure success of conventional ablation in recent reports is less encouraging. The 92% single FIRM-guided procedure 2-year freedom from AF/AFL in this study is higher than the 50-60% single procedure success of conventional ablation in recent reports of paroxysmal AF including the use of contact force sensing and recent balloon technologies. Similarly, in a recent meta-analysis of catheter ablation outcomes, it was determined that the single procedure success of conventional ablation for persistent AF was a disappointing 41.8%. After an average of approximately 1.7 procedures per patient, multiple procedure success of conventional ablation for persistent AF increased to 77%, which is similar to the single FIRM-guided procedure 79% 2-year freedom from AF/AFL for persistent AF reported in this investigation.

Of note, FIRM-guided ablation in paroxysmal AF may provide a means to improve success over the rates cited above in recent trials, while potentially reducing the extent of ablation since nearly all of those trials included substantial extra-PVI ablation. For instance, patients with paroxysmal AF in RAAFT-2 had CFAE ablation in 17% and roof lesions in 21.3%.

The repeat AF ablation population

Recurrent AF/AFL following PVI is unfortunately a frustrating and common clinical problem. The need for additional ablations, which do not guarantee success, increases both expense and procedural risks. In both the multicenter registry and in our investigation, ~48% of the patients studied had previous AF ablations. The 72% long-term freedom from AF/AFL in this study for the repeat FIRM-guided ablation patients is again remarkably consistent with the 73% and 68% 1-year freedom from AF and all atrial arrhythmias seen in the multicenter registry. Despite a lower percentage (22%) of repeat ablation patients, even the 3-year follow-up CONFIRM trial data of previously ablated patients achieved better results than conventional therapy. Repeat ablation patients in our study had the same number of AF terminations and long-term success, as did the first ablation group. Interestingly, 80% of repeat ablation patients with more than two previous ablations remained in sinus rhythm at 2 years off medications. These results would suggest that FIRM-guided ablation can improve success rates in this common patient population. Prospective randomized trials would help to determine if future strategies for the repeat AF ablation population should include FIRM ablation.

Limitations

The main limitations of this study are the relatively small number of patients and the lack of a control group undergoing conventional ablation alone for a true comparison of the long-term effectiveness of FIRM-guided ablation. Historically speaking, however, long-term single procedure freedom from AF/AFL in similar AF patient populations with conventional ablation alone has been less than 50%. While these results are promising, the question of how the success rates of FIRM-guided substrate ablation compare with conventional ablation still require multicenter randomized trials which are ongoing.

An additional limitation is the lack of a randomization protocol involving multiple arms for RFCA, which is presently being addressed in multicenter randomized controlled trials. Although both AT and AF were seen on
follow-up, our high overall phase II single FIRM-guided procedure freedom from AF and AT of 74.7% (59/79) shows that these atrial tachycardias would not traditionally be considered pro-arrhythmic.

The main limitations of FIRM mapping and ablation in its present state include poor basket electrode contact, inadequate RA/LA electrode tissue coverage, lack of real-time visualization of rotor activity to see the direct effects of RFA on rotor core, and the need for standardized ablation strategies for rotor elimination.

Conclusions

In a single-center non-randomized study, FIRM-guided RFCA of AF demonstrated promising high 2-year freedom from AF and AFL rates when performed in addition to antral PVI in a complex patient population who historically have been refractory to conventional ablation alone. The high freedom from AF and AFL rates existed for both first and repeat ablation patients both with paroxysmal and persistent AF. The results of this study strongly warrant randomized control trials.

References


