Received: 7 February 2017 | Revised: 28 March 2017 | Accepted: 20 April 2017
DOI: 10.1111/jce.13240

ORIGINAL ARTICLE

WILEY

Type and rate of atrial fibrillation termination due to rotational activity ablation combined with pulmonary vein isolation

Zsuzsanna Kis MD | Dominic A. Theuns PhD, FESC | Rohit Bhagwandien MD | Sip Wijchers MD | Sing-Chien Yap MD, PhD | Tamas Szili-Torok MD, PhD

Department of Electrophysiology, Erasmus MC, University Medical Center, Rotterdam, the Netherlands

Correspondence
Tamas Szili-Torok, MD, PhD, Thoraxcenter, Department of Clinical Electrophysiology, Erasmus MC, Postbus 2040, 3000 CA Rotterdam, The Netherlands, 's Gravendijkwal 230.
Email: t.szilitorok@erasmusmc.nl

This manuscript was processed by a guest editor.

Disclosure: Dr. Szili-Torok reports a research fellowship grant sponsored by Abbott, and serving on the advisory board ofan undisclosed company. Other authors: No disclosures.

Abstract

Background: There remains controversy about the optimal ablation technique and termination rate of atrial fibrillation (AF) during catheter ablation in patients with persistent AF. The aim of this study was to determine the rate and timing of AF termination during combined pulmonary vein isolation (PVI) and focal impulse and rotor modulation (FIRM)-guided ablation of rotational activity (RoAc).

Methods: This single-center, prospective cohort study enrolled 38 consecutive patients (63% male, mean age 63 ± 11 years) with persistent AF (mean left atrial size: 46 ± 7 mm), who underwent FIRM mapping and ablation of the identified RoAcs followed by PVI. We systematically evaluated the incidence and timing of AF termination during AF ablation.

Results: "Late-onset termination" of AF could be observed in 12 (32%) patients after ablation of the identified RoAcs. In a further 10 (26%) patients, "abrupt" AF termination during PVI was achieved. In total, the combined technique of conventional PVI and RoAc ablation resulted in AF termination rate of 58%. ECV was performed in 16 "nonterminating" patients. At 1-year follow-up, 76.1% (16 of 21) of patients remained free from AF/AT, 4 of 10 patients (25%) within the "abruptly" terminated group, 7 of 12 (58.3%) patients among the "late-terminated" group, and 5 of 16 (31, 25%) patients in the "nonterminating" group.

Conclusion: Large area RoAc ablation combined with PVI results in a moderate termination rate of persistent AF with two distinctive timing patterns. More studies are needed to determine the clinical significance of type of AF termination and long-term success rate of RoAc ablation in patients with persistent AF.

KEYWORDS
ablation outcome, FIRM-guided rotor ablation, persistent atrial fibrillation, pulmonary vein isolation, type of atrial fibrillation termination

1 | INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia resulting in the reduction of quality of life, functional clinical status and overall survival.[1,2] Although several basic and clinical studies demonstrated that pulmonary vein isolation (PVI) is superior to medical therapy in AF management, the underlying mechanism of PVI efficacy is still not completely clear.[3–6] Haïssaguerre et al. detected that pulmonary veins (PVs) have a role in triggering of AF. However, our knowledge about AF drivers responsible for AF maintenance is still far from being complete.[7] One can assume if a driver of AF is eliminated then it should result in termination and/or noninducibility of the arrhythmia. PVI provides a generic anatomical approach to eliminate AF triggers and also the susceptive driver(s) in PVs as well. Recently, the focal impulse and rotor modulation (FIRM) mapping became available, which aims to identify areas of the atria functioning as patient-specific AF driver(s).[8–10] Targeting these atrial substrates ensures a patient-tailored ablation strategy for AF elimination.[11] Despite this, the clinical outcome data of AF termination after FIRM-guided ablation are still controversial.[9,12,13] The aim of the current study was to evaluate the timing and rate of AF termination using ablation of rotational activity (RoAc) detected by FIRM mapping combined with conventional PVI in persistent AF patients.

2 | METHODS

2.1 | Study population

This single-center, prospective study enrolled 38 consecutive patients with symptomatic persistent AF despite pharmacologic therapy and/or prior ablation undergoing a combined conventional PVI and FIRM-guided ablation between March 2015 and April 2016. Persistent AF was defined as continuous AF that is sustained beyond 7 days. Episodes of AF in which a decision was made to electrically or pharmacologically cardiovert the patient after ≥48 hours of AF, but prior to 7 days, were also be classified as persistent AF episodes."[1] Written informed consent was obtained from all patients. Data collection for this study was approved by the institutional review board and the ethical committee. We did not include patients with paroxysmal AF and those with presence of intracavital thrombus. Patients with pacemaker or with implantable cardiac defibrillator were not scheduled for the procedure. None of the patients suffered from longstanding AF.

2.2 | Electrophysiologic study

The electrophysiologic study was performed without interrupting the antiarrhythmic drug (AAD) therapy. Of note, this is our AAD policy for persistent and longstanding persistent AF ablation procedures. Decapolar catheters were advanced via femoral venous access to the coronary sinus. If spontaneous AF was not observed, AF was induced by burst pacing starting at 500 milliseconds cycle length (CL) and reduced with 50 milliseconds steps to 300 milliseconds, then reduced with 10 milliseconds until initiation of AF. Sustained AF after >10 minutes of duration was mapped. Intravenous heparin was administered to reach ACT > 300 seconds before introduction of the basket catheter. A 64-pole basket catheter spaced along eight splines (FIRMap, Abbott, Chicago, IL, USA) was passed through an 8.5 Fr SL1 sheath to identify RoAc firstly in the right atrium. Sizing and positioning of the basket catheter such as the confirmation of good atrial contact was ensured by fluoroscopy and/or intracardiac echocardiography (ICE). After identification and elimination of all right-sided RoAcs we placed the basket catheter through ICE-guided transseptal puncture to the left atrium. If all identifiable RoAcs were eliminated we continued the procedure with PVI. If AF termination could not be reached during RoAc ablation then PVI was performed in AF. At the end of the procedure in case of unsuccessful ECV we rechecked the PV reconnections as well.

2.3 | FIRM mapping and AF sources

AF was recorded using wide field of view basket catheters. Unipolar and bipolar intracardiac signals from the basket catheter were filtered at 0.05–500 Hz and recorded at 1-kHz sampling frequency for export from the electrophysiology recording system to the computational FIRM-mapping system (RhythmView, Topera, San Diego, CA, USA). This system first preprocessed the electrograms to remove the QRS signals to improve the signal-to-noise ratio.[12,14] The system then analyzed the AF cycles at each electrodes over successive timepoints. The resulting computational phase map depicts the putative propagation of electrical activity of AF.[12] The AF propagation maps are then projected onto a two-dimensional (2-D) grid. The 2-D grid portrays the right atrium opened through the tricuspical annulus vertically, while representing the left atrium opened horizontally through the mitral valve.[12] The location of the rotors and focal sources could be identified by their electrode coordinates based on three-dimensional (3-D) electroanatomic map.[14] In the present study, NavX (St. Jude Medical, St Paul, MN, USA) 3-D electroanatomic mapping system was used. RoAc was defined as sustained clockwise or counterclockwise activation around a core, or a centrifugal activation from an origin, which were located on the basis of their electrode coordinates.[15–17] The basket coverage was confirmed in all cases by fluoroscopy and/or ICE, electrograms quality checking and basket visualization on the 3-D mapping system. If poor signal quality was achieved, then repositioning of the basket catheter was executed until adequate raw signals could be recorded. The assessment of the RoAc based on the results of rotational activity profile (RAP) software tool of the Topera system. It could be overruled if the quality of raw signals appeared to be inadequate or if RoAc was not clearly identifiable. All effort was done to determine whether each RoAc was reproducible over several 4-second epochs. The stability of RoAc ensures a rational target for limited ablation. The RAP tool provides easier detection of areas that have more RoAc. Areas of higher RoAc for selected time segments are highlighted superimposed on the relevant grid locations.

2.4 | Ablation procedure

In all included patients, FIRM-mapping and RoAc ablation was performed prior to PVI. If FIRM-mapping revealed RoAc, then a FIRM-guided ablation was executed first in the right then in the left atrium. Subsequently, conventional PVI-only was performed.

Only RoAc(s) identified by the RAP feature with a repetitive, spatially stable rotational pattern from the default 4-second time segment were targeted for ablation, except if considered to be a false positive upon a visual assessment of the operator. Using 3.5-mm irrigated-tip catheters radiofrequency energy was applied to the basket grid coordinates, referenced to electrode positions on electroanatomic shells. The power setting was <25 W for the posterior atrial wall and 40 W for the rest of atria, the temperature limit was set to 43 C°. In FIRM-guided ablation the RF applications were applied directly to center ofthe RoAc bounded by ≈2 electrodes distance in each axis for around 300 seconds in each side.[16] AF terminated rigorous attempts were used in all patients to re-induce AF using pacing maneuvers protocol for AF initiation. The definition of re-inducibility was to be >30 seconds duration of sustained AF. If AF was reinduced, then a novel FIRM mapping was indicated. Each additional RoAc sites were similarly ablated until all identifiable RoAc were eliminated based on repeated FIRM maps. Verification of the PVI was implemented in all patients using a circular mapping catheter (LassoNav™, Biosense Webster Inc., Diamond Bar, CA, USA) after conventional PVI. If AF organized into atrial flutter or tachycardia, then these were treated with application of the appropriate line(s). Additional substrate ablation (roof or mitral isthmus line, non-PV sources) was not routinely accomplished. Electric cardioversion

(ECV) was performed only in the absence of conversion to sinus rhythm (SR) after completion of the ablation protocol.

2.5 | Follow-up

Patients were seen at the outpatient clinic following a 3-month blanking period at postablation 3, 6, and 12 months. During these visits, 12-lead ECGs were obtained. In addition, long-term monitoring was obtained by trans-telephonic ECG monitoring between 3 and 4, and between 6 and 7 months postablation. At 6 and 12 months follow-up, 7-day Holter-recordings were obtained. Between the 6 and 12 months of follow-up, symptom-driven event monitoring was ensured if required. Arrhythmia recurrence was defined as any episode of documented AF/AT > 30 seconds.

2.6 | Study endpoints

The prespecified primary efficacy endpoint was the rate and timing of AF elimination during the combined RoAc and PVI ablation procedure. Secondary endpoint was safety, defined as incidence of periprocedural complication(s).

2.7 | Statistical analysis

Normality of distribution was assessed using with the Shapiro-Wilks test. Continuous variables are presented as mean ± standard deviation (SD), if normally distributed, otherwise by median and corresponding 25th and 75th percentile. Data were compared by the ANOVA or Mann-Whitney U test, as appropriate. Categorical variables are expressed as number and percentage (%) and compared with Fisher's exact test. Logistic regression analysis was performed to study the relation between clinical covariates and the type of termination of AF during rotor ablation. The following covariates were considered as presumable predictors of AF termination: AF duration, AF type, rhythm before ablation, location of the rotors. Statistical analysis was performed using SPSS version 21 (IBM Corp., Somers, NY, USA). Statistical significance was defined as $P < 0.05$ (two-tailed).

3 | RESULTS

3.1 | Patient characteristics

Baseline clinical and demographic data are summarized in Table 1. The majority of the patients were male (63%) and had undergone a prior PVI (53%). The mean AF time since the diagnosis before the combined AF ablation procedure was 4.5 ± 3.2 years. The CHA_2DS_2VaSc score was 1.8 ± 1.2 and the mean left atrial size was 46 ± 7 mm in diameter. All patients had persistent AF. There were 14 patients (37% of the cohort) who arrived in SR for the ablation due to ECV prior to procedure despite classified as persistent AF patients previously. None of the patients in this patient cohort had longstanding AF. AAD medication was continued during the ablation procedures. Based on the Singh-Vaughan Williams classification, 7 patients were on class I medication, class II drugs were administered in 16 patients, while 19 patients were on class III drugs and 5 patients were treated with digoxin. Following the 3-month blanking period the class III drugs were discontinued in 11 patients, while the class II drugs and/or digoxin were stopped in further 4 patients. At the 6-month follow-up,

TABLE 1 Demographic, clinical and procedural data of the patient cohort

Age (years)	63 ± 11
Sex (M)	24/38 (63%)
AF duration (years)	4.5 ± 3.2
Prior pulmonary vein isolation	20/38 (53%)
Hypertension	21/38 (55%)
Hyperlipidemia	8/38 (21%)
Diabetes mellitus	6/38 (16%)
Sleep apnea	3/38 (8%)
COPD	2/38 (5.2 %)
Pulmonary hypertension	0/38
Left atrial appendage size (mm)	46 ± 7
CHA_2DS_2VASC-score	1.8 ± 1.2
Ischemic heart disease	6/38 (16%)
Dilated cardiomyopathy	4/38 (11%)
Body mass index	28.4 ± 3.8
Type of AF (nonparoxysmal)	38/38 (100%)
AF initiation required at the beginning of the procedure	14/38 (37%)
Rotational activity found	30/38 (79%)
Number of left-sided RoAc per patient	0.7 ± 0.8
Number of right-sided RoAc per patient	1.4 ± 1.7
Patients with left-sided RoAc	18/38 (47%)
Patients with right-sided RoAc	27/38 (71%)
Abrupt termination of AF during PVI RF delivery	10/38 (26%)
Late-onset termination of AF	12/38 (32%)
Restoration to sinus rhythm due to ablation	22/38 (58%)
ECV required at the end of the procedure	16/38 (42%)
Fluoroscopy time (minutes)	34 ± 11
Procedure time (minutes)	282 ± 62
Radiofrequency application duration (seconds)	2,189 ± 1,188
Cavotricuspidal isthmus ablation	5/38 (13%)
Organization to AT	4/38 (10%)
Reconnected PVs after prior PVI (n)	2.4
Complications	4/38 (11%)
Groin hematoma	3/38 (8%)
Left atrial appendage thrombus formation	1/38 (3%)

*AF = atrial fibrillation, +CHA_2DS_2VASC-score = risk stratification for stroke of AF patients, ++AT = atrial tachycardia, ‡ECV = electric cardioversion, §SR = sinus rhythm, II PVI = pulmonary vein isolation, #RoAc = rotational activity, **COPD = chronic obstructive pulmonary disease.

class III drugs in 7 patients and class II drugs in further 5 patients were withdrawn.

3.2 | Procedural characteristics

Procedural data are summarized in Table 1. SR was presented in 37% of patients (n = 14) at the beginning of the procedure, requiring induction of AF. Preparation time for left atrial access took 3–15 minutes after RA RoAc ablation and generally 3–10 minutes between LA RoAC ablation and PVI. Electrical RoAc were seen in 30 of 38 (79%) patients, with a mean of 0.7 ± 0.8 in the left atrium and a mean of 1.4 ± 1.7 in the right atrium per patient. Left atrial RoAc were identified in 18 patients (47%), while in 27 patients (71%) right-sided RoAc were detected. PVI was not performed in 1 of 20 patients who previously underwent AF ablation because PVs were still completely isolated. Pulmonary vein reconnections were revealed in a majority of patients (93%) who had undergone prior AF ablation with a mean of 2.4 reconnected PVs; all of these were reisolated. Cavotricuspidal isthmus ablation was performed in 5 (13%) patients. The average procedure duration was 282 ± 62 minutes with an average of 34 ± 11 minutes fluoroscopy time, and 2,189 ± 1,188 seconds of radiofrequency application duration. The size of the basket was selected based on the LA diameter measured by preprocedural TEE and/or ICE. In 21 patients (55.3%) the 50 mm, while in 17 patients (44.7%) the 60 mm basket size was used. The 70-mm basket size was not utilized in this patient cohort. In the right atrium the basket coverage was generally complete, implied by identical spline spacing and balanced basket deployment visualized with fluoroscopy. A segmental mapping and ablation if required was implemented to adjust incomplete basket coverage.

3.3 | Timing of AF termination

Two distinctive types of the AF termination were defined. The "abrupt termination" of AF presented during PVI RF delivery. It was tended to be more present among patients without RoAc (P = 0.051; Fig. 2) The "late-onset termination" of AF occurring between 3 minutes and 24 hours following RoAc activity ablation was significantly more prevalent in patients with right-sided RoAc (P = 0.049; Fig. 3). The mean time of "late-onset termination" (excluding the one with 24 hours termination) was 13.8 ± 4 minutes after RoAc ablation.

3.4 | Rate of AF termination

The overall termination of AF after combined RoAc ablation with PVI was observed in 22 out of 38 patients (58%; Fig. 1). AF terminated abruptly during PVI RF delivery in 10 out of 38 patients (26%). Late-onset termination was observed in 12 (32%) patients after RoAc ablation (ranging between 3 minutes and 24 hours).

AF organization to atrial tachycardia during ablation was observed in a further 4 patients (10%), in whom SR was achieved with additional linear line ablation and ECV. These patients were counted in the "nonterminating group" of patients. ECV was attempted in 16 patients

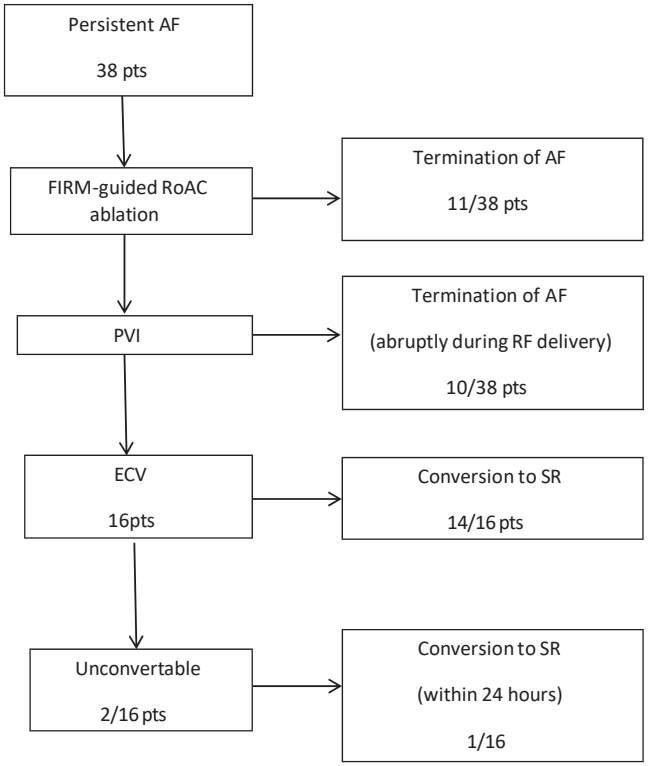

FIGURE 1 Rate and timing of AF termination during FIRM-guided ablation combined with PVI *AF = atrial fibrillation, +FIRM = focal impulse and rotor modulation, ‡RoAc = rotational activity, §PVI = pulmonary vein isolation, II ECV = electrical cardioversion, #SR = sinus rhythm

(42%) at the end of the ablation procedure. Fourteen of them were electrically converted to SR, while 2 patients remained unconvertible. One patient out of them converted to SR within 24 hours after ablation. Elimination of all RoAcs and isolation of all PVs was reached in 37 of 38 patients (95%). In 1 patient, the RoAc was not ablated due to its proximity to the compact AV node. Based on the statistical analysis no difference was observed in termination rate among patients who had had prior PVI compared to those who underwent the first PVI procedure combined with FIRM mapping. Also, no differences were observed in termination rate if AF was induced at the beginning of the procedure or if the patient arrived to the lab in AF.

3.5 | Complication

Procedural complication occurred in 3 cases (9%) presenting with groin hematoma; in another patient (3%) left atrial appendage thrombus formation was revealed by transesophageal echocardiography performed right after the ablation for guiding the planned appendage closure procedure.[18]

3.6 | Predictor of AF termination

In univariate analysis, no association between covariates including AF duration, AF type, rhythm before ablation, location of the rotors was found with the type of AF termination.

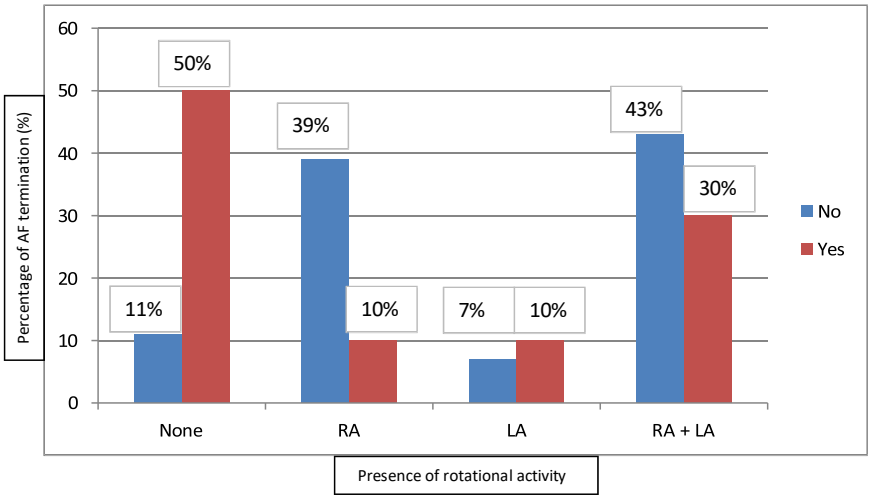

FIGURE 2 Abrupt termination of atrial fibrillation tended to be more present in patients without identifiable rotational activity n = 10 (P = 0.051) *RA = right atrium, +LA = left atrium, ‡RA + LA = right + left atrium, # None = patients without rotational activity [Color figure can be viewed at wileyonlinelibrary.com]

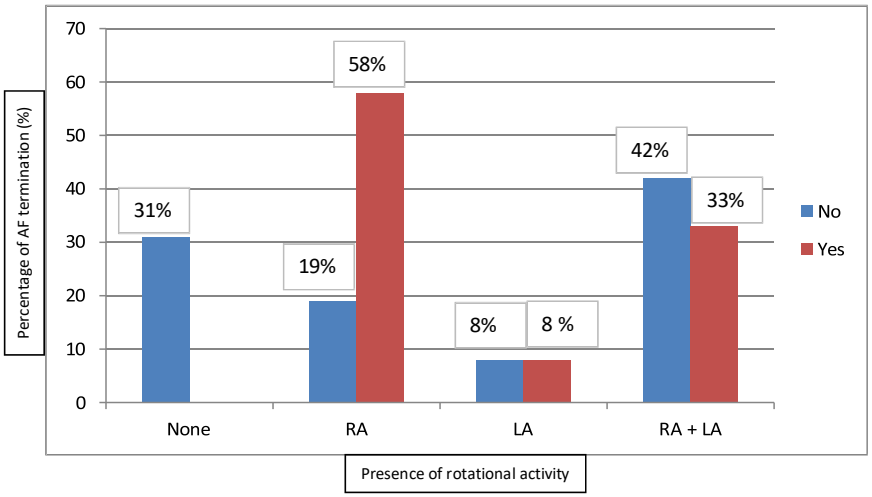

FIGURE 3 Late-onset termination of atrial fibrillation was more prevalent in patients with right-sided rotational activity n = 12 (P = 0.049) *RA = right atrium, +LA = left atrium, ‡RA + LA = right + left atrium, #None = patients without rotational activity [Color figure can be viewed at wileyonlinelibrary.com]

3.7 | Follow-up

Follow-up data with 3-month blanking period were available for all studied patients. At 3 months of follow-up, 26.3% (10 of 38) of the patients presented with early arrhythmia recurrence. At 6-month follow-up, 63.88% (23 of 36), while at 12-month follow-up, 76.1% (16 of 21) of patients remained free from AF/AT. The 1-year outcome data include 3 patients with ECV and 3 patients who underwent re-ablation (1 with CTI, 2 with redo PVI + FIRM-guided ablation) between the 6- and 12-month FU visits, with 5 patients remaining on at least a reduced dose of a previously ineffective antiarrhythmic medication. The 1-year single-procedure success rate was 69.1% (13 of 21). Figure 4 demonstrates the outcome flowchart at each time interval. At 1-year follow-up freedom from AF/AT was detected in 4 out of 10 patients (25%) within the "abruptly" terminated group, while in 7 of 12 (58.3%) patients in the "late-onset terminated" group and in 5 of 16 (31, 25%) patients in the "nonterminating" group. Neither termination of AF to SR itself nor the termination type predicted the arrhythmia free survival at 1-year follow-up.

4 | DISCUSSION

The major finding of our study is a moderate rate (58%) of persistent AF termination with two distinctive timing pattern following FIRM-guided ablation combined with PVI. The "late-onset termination" of AF is significantly more prevalent in patients during right-sided RoAc ablation. The "abrupt termination" of AF is tended to be more present among patients during PVI. Termination does not depend on whether AF is induced or ongoing at the beginning of the procedure.

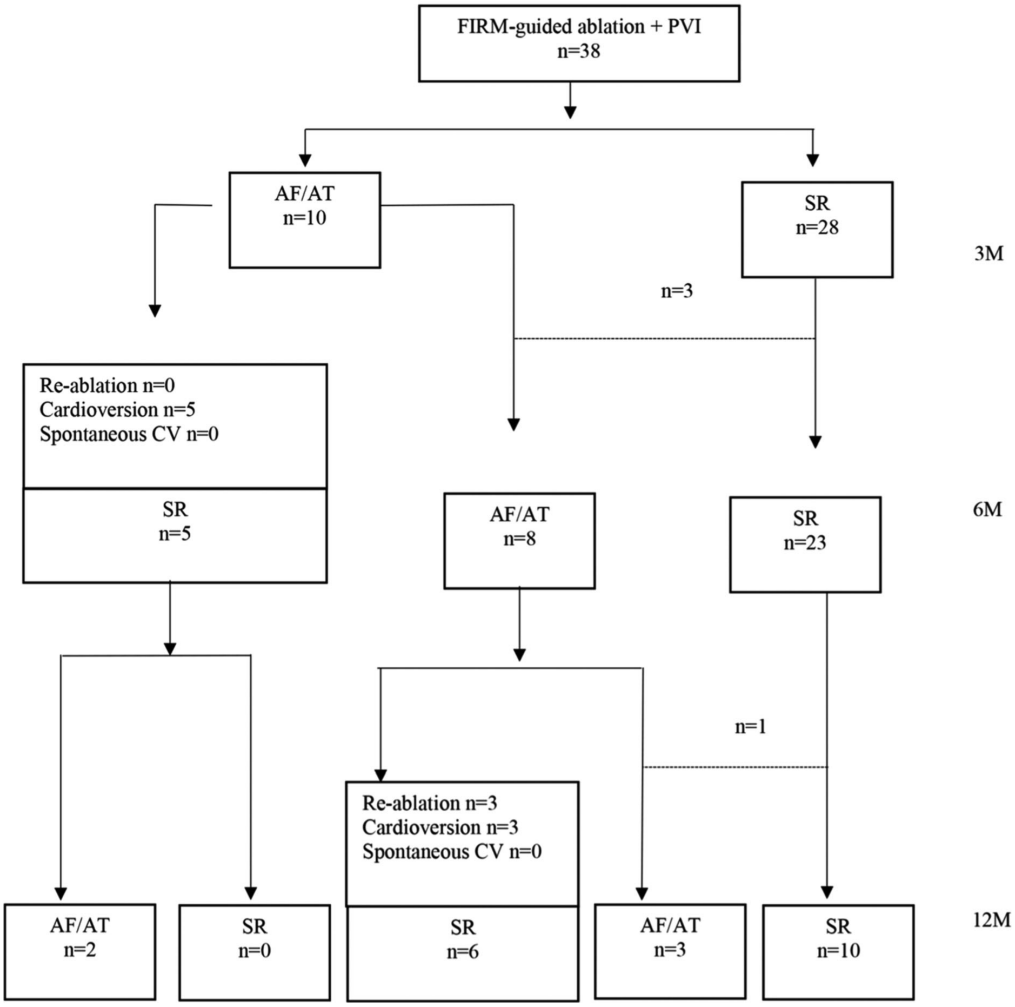

FIGURE 4 Arrhythmia outcome flowchart showing arrhythmia-free survival at 3-, 6-, 12-month time intervals. PVI = pulmonary vein isolation, SR = sinus rhythm, AF = atrial fibrillation, AT = atrial tachycardia, FU = follow-up, CV = cardioversion 3M: 3-month arrhythmia free survival FU - 73.68% (28 of 38) 6M: 6-month arrhythmia free survival FU - 63.88% (23 of 36) 12M: 12-month arrhythmia free survival FU - 76.1% (16 of 21)

4.1 | Drivers of AF

If we agree that elimination of AF drivers should result in termination of AF such as in other arrhythmias, then if we could individually define the AF substrate(s) we should be able to reach more promising long-term results even in persistent AF patients with catheter ablation.

Nowadays, identification of RoAc susceptive of sustaining human AF represents a novel option for catheter ablation approach. Elimination of FIRM-detected RoAcs provides a patient-specific ablation method; however, a great debate is going on why AF does not acutely terminate after RoAcs ablation. Schricker et al. reported different possible hypothesis on this topic. First, due to the limitation of the current FIRM-mapping system certain RoAc may remain hidden in the unmapped area of the atria. Second, the time period that fibrillatory conduction can sustain AF without driver is still questionable. It may last from seconds to hours.[16] It is still unclear how localized ablation effects on RoAc and what mechanisms lead to the termination of AF. The recent optical mapping studies by Fedorov et al. on human ex vivo heart demonstrated that intramural microanatomic reentry circuits stabilized by microanatomic substrates can maintain AF. Endocardial catheter ablation of these microanatomic reentries stopped AF, suggesting the human 3-D atrial architecture may have a key role in the AF maintanance.[19] Further studies are necessary to address these mechanistic questions.

Our results suggest that the two distinctive timing patterns of AF elimination is derived from individual location and mechanism of AF driver(s). The "late-onset termination" of AF occurring between 3 minutes and 24 hours following RoAc activity ablation was significantly more prevalent in patients with right-sided RoAc. Abrupt AF termination during PVI delivery tended to be more present among patients without RoAc. Our results emphasize that the PVs have a role not only in triggering but also in driving AF.

4.2 | Termination of AF

All in all, only 79% (30 of 38) of patients had identifiable RoAc in this study, with a lower number of RoAc per patients but with a higher right-sided prevalence compared to previous FIRM-guided AF ablation studies.[12,13,15] The slightly high number of patients without

identifiable RoAc (21%) might derive from the technical limitation of the mapping system. The higher percentage of right atrial RoAc(s) in this study is in line with the findings published by Fedorov et al.[20] They demonstrated first in ex vivo human atria with optical mapping experiments that a near three-fold greater right atria (RA)-to-left atria (LA) adenosine A1 receptor protein expression (specially in superolateral RA region) leads to significantly greater RA versus LA repolarization sensitivity in response to adenosine. Sustained adenosine-induced AF was maintained by localized reentrant drivers in the superior/middle lateral RA, where the shortest action potential duration and the highest A1 receptor expression were observed.[20]

The AF termination rate to SR in our study (58%) is comparable with the results of a CONFIRM trial, in which 56% (20 of 36 cases) AF termination rate was reported.[15] Narayan et al. reported that procedural success was more prevalent in those patients who required AF initiation at the beginning of the procedure.[15] In our study, the investigated covariates, including the rhythm prior ablation, was not associated with the type of AF termination. In the first multicenter, nonrandomized study the acute endpoint of AF termination was achieved in 67% (8 of 14 cases).[12] Tilz et al. reported on 12 (48%) patients either with AF termination (24% = 6 of 25) or with conversion to another rhythm, or CL prolongation ≥10% after rotor ablation.[21] On the contrary, lower spontaneous procedural termination rate was observed in 8.6% of patients (5 of 58) reported by Spitzer et al. and only in 1 out of 20 patients terminated to SR during ablation in the study by Sommer et al.[22,23]

4.3 | Clinical outcome

In the present study, 38 patients with nonparoxysmal AF after FIRM-guided RoAc ablation combined with PVI demonstrates 76.1% (16 of 21) freedom from AF/AT with 12-month follow-up with 5 patients on AAD therapy, while our 1-year single-procedure success rate was 69.1% (13 of 21). This is consistent with several previously reported clinical outcome data.[13,21–24] Miller et al. reported 80.5% 1-year freedom for AF in a 10-center independent registry.[13] In addition, Spitzer et al. published a similar 73.1% arrhythmia-free survival after a single FIRM-guided procedure with 12-month follow-up, while Tilz et al. reported on 52% single procedure success rate with 13 ± 1 months follow-up.[21,22] In the study published by Sommer et al., a single-procedure freedom from AF was 80% after a follow-up of 6 months, with 1 patient on dronaderone and with all remaining patients being on beta-blocker. Our results are more promising than the 38% arrhythmia-free survival reported by Buch et al., which might be explained by different factors: their difficulties in basket placing, application of the precommercial version of the Rythm View software, challenging patient cohort.[25]

Some studies demonstrated that the lower spontaneous procedural termination was not predictive of long-term outcomes; on the contrary, rotor elimination was associated with favorable long-term clinical outcome.[22,23] The present study is in line with these findings, as 5 out of 16 patients (31%) within the "nonterminating" group presented with SR at 1-year follow-up. The observation that the success rate of FIRM-guided ablation might increase over time may derive from the reverse remodeling. The FIRM-guided rotor ablation changes not only substrate but also may render the substrate to be less vulnerable to AF triggers.

4.4 | Study limitation

This study has several limitations. First, the present study includes the relatively small sample size and lack of control group who underwent exclusively PVI-only ablation alone. The ongoing REAFFIRM study will help us to compare the outcome data of persistent AF patients after conventional PVI versus conventional + FIRM-guided ablation. The small sample size prohibits the identification of predictors of AF termination. Second, we cannot exclude that previous procedures might have had impact on RoAcs. Additionally, there may be technical limitations derived from computational approaches for rotor mapping. Further improvements in the design and the resolution of FIRM-mapping system are required to provide better outcome with FIRM-guided ablation. The present study was not powered to assess the potential effect of AAD medication on the outcome of the ablation procedure.

4.5 | Clinical implication

FIRM mapping offers a novel and feasible technique for identification of RoAc sustaining human AF. Furthermore, this technique provides a patient-tailored, mechanistically focused method for catheter ablation of AF. Further prospective, randomized controlled studies are needed to define the precise mechanism of AF termination during FIRM-guided ablation combined with PVI.

In conclusion, this is the first study observing moderate rate and two distinctive timing patterns of persistent AF termination during FIRM-guided RoAc ablation combined with conventional PVI. Abrupt termination of persistent AF was achieved with higher probability in those presented without RoAc. The late termination of AF was significantly more prevalent in patients with right-sided RoAc.

REFERENCES

1. Calkins H, Kuck KH, Cappato R, et al. 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. *Europace*. 2012;14:528–606.
2. Fuster V, Ryden LE, Cannom DS, et al. American College of Cardiology, American Heart Association Task Force, European Society of Cardiology Committee for Practice Guidelines, European Heart Rhythm Association, Heart Rhythm Society. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: full text: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 guidelines for the management of patients with atrial fibrillation) developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Europace*. 2006;8:651–745.
3. Hakalahti A, Biancari F, Nielsen JC, Raatikainen MJ. Radiofrequency ablation vs. antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: Systematic review and meta-analysis. *Europace*. 2015;17:370–378.

4. Morillo CA, Verma A, Connolly SJ, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation (RAAFT-2): A randomized trial. *JAMA*. 2014;311:692–700.
5. Wazni OM, Marrouche NF, Martin DO, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: A randomized trial. *JAMA*. 2005;293:2634–2640.
6. Wilber DJ, Pappone C, Neuzil P, et al. ThermoCool AFTI. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: A randomized controlled trial. *JAMA*. 2010;303:333–340.
7. Haissaguerre M, Jaïs P, Shah DC. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N EnglJ Med*. 1998;339:659–666.
8. Zaman JA, Narayan SM. Ablating atrial fibrillation: Customizing lesion sets guided by rotor mapping. *Methodist Debakey Cardiovasc J*. 2015;11:76–81.
9. Narayan SM, Baykaner T, Clopton P, et al. 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;63:1761–1768.
10. Baykaner T, Clopton P, Lalani GG, et al. Investigators C. Targeted ablation at stable atrial fibrillation sources improves success over conventional ablation in high-risk patients: A substudy of the CONFIRM Trial. *Can J Cardiol*. 2013;29:1218–1226.
11. Benharash P, Buch E, Frank P, et al. Quantitative analysis of localized sources identified by focal impulse and rotor modulation mapping in atrial fibrillation. *Circ Arrhythm Electrophysiol*. 2015;8:554–561.
12. Shivkumar K, Ellenbogen KA, Hummel JD, Miller JM, Steinberg JS. Acute termination of human atrial fibrillation by identification and catheter ablation of localized rotors and sources: First multicenter experience of focal impulse and rotor modulation (FIRM) ablation. *J Cardiovasc Electrophysiol*. 2012;23:1277–1285.
13. Miller JM, Kowal RC, Swarup V, et al. Initial independent outcomes from focal impulse and rotor modulation ablation for atrial fibrillation: Multicenter FIRM registry. *J Cardiovasc Electrophysiol*. 2014;25:921–929.
14. Narayan SM, Krummen DE, Rappel WJ. Clinical mapping approach to diagnose electrical rotors and focal impulse sources for human atrial fibrillation. *J Cardiovasc Electrophysiol*. 2012;23:447–454.
15. Narayan SM, Krummen DE, Shivkumar K, Clopton P, Rappel WJ, Miller JM. Treatment of atrial fibrillation by the ablation of localized sources: CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) trial. *J Am Coll Cardiol*. 2012;60:628–636.
16. Schricker AA, Zaman J. Role of rotors in the ablative therapy of persistent atrial fibrillation. *Arrhythm Electrophysiol Rev*. 2015;4:47–52.
17. Walters TE, Kalman JM. Human persistent atrial fibrillation is maintained by rotors: The jury is still out. *Circ Arrhythm Electrophysiol*. 2015;8:517–519.
18. Kis Z, Bhagwandien R, Nieman K, Wijchers S, Szili-Torok T. Left atrial appendage thrombus formation during atrial fibrillation ablation under sufficient heparinization. *Europace*. 2016;18:1800.
19. Hansen BJ, Zhao J, Csepe TA, et al. Atrial fibrillation driven by micro-anatomic intramural re-entry revealed by simultaneous sub-epicardial and sub-endocardial optical mapping in explanted human hearts. *Eur Heart J*. 2015;36:2390–2401.
20. Li N, Csepe TA, Hansen BJ, et al. Adenosine-induced atrial fibrillation: Localized reentrant drivers in lateral right atria due to heterogeneous expression of adenosine A1 receptors and GIRK4 subunits in the human heart. *Circulation*. 2016;134:486–498.
21. Tilz RR, Lin T, Rillig A, et al. Focal impulse and rotor modulation for the treatment of atrial fibrillation: Locations and 1 year outcomes of human rotors identified using a 64-electrode basket catheter. *J Cardiovasc Electrophysiol*. 2017;28:367–374.
22. Spitzer SG, Karolyi L, Rammler C, et al. Treatment of Recurrent Nonparoxysmal Atrial Fibrillation Using Focal Impulse and Rotor Mapping (FIRM)-guided rotor ablation: Early recurrence and long-term outcomes. *J Cardiovasc Electrophysiol*. 2017;28:31–38.
23. Sommer P, Kircher S, Rolf S, et al. Successful repeat catheter ablation of recurrent longstanding persistent atrial fibrillation with rotor elimination as the procedural endpoint: A case series. *J Cardiovasc Electrophysiol*. 2016;27:274–280.
24. Narayan SM, Krummen DE. Treatment of atrial fibrillation by the ablation of localized sources: CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and and Rotor Modulation) trial. *Am Coll Cardiol*. 2012.
25. Buch E, Share M, Tung R, et al. Long-term clinical outcomes of focal impulse and rotor modulation for treatment of atrial fibrillation: A multicenter experience. *Heart Rhythm*. 2015;13:636–641.

How to cite this article: Kis Z, Theuns DA, Bhagwandien R, Wijchers S, Yap S-C, Szili-Torok T. Type and rate of atrial fibrillation termination due to rotational activity ablation combined with pulmonary vein isolation. *J Cardiovasc Electrophysiol*. 2017;28:862–869. https://doi.org/10.1111/jce.13240