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Impact of Rotor Ablation in Nonparoxysmal Atrial Fibrillation Patients

Results From the Randomized OASIS Trial

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ABSTRACT

BACKGROUND Nonrandomized studies have reported focal impu[illegible]nd r[illegible]or modula[illegible]on (FIRM)-guided ablation to be superior to pulmonary vein antrum isolation (PVAI) for persi[illegible]ent atria[illegible]illation [illegible] long-standing persistent atrial fibrillation.

OBJECTIVES This study sought to compare efficacy o[illegible]IRM ab[illegible]on with or without PVAI versus PVAI plus non-PV trigger ablation in randomized persistent atrial fibrillation and long-st[illegible]ing persistent atrial fibrillation patients.

METHODS Nonparoxysmal atrial fibrillation (A[illegible] patients undergoing first ablation were randomized to FIRM only (group 1), FIRM + PVAI (group 2) or PVAI + po[illegible]erior wall + no[illegible]PV trigger ablation (group 3). Primary endpoint was freedom from atrial tachycardia/AF. The second[illegible]y endpoint was [illegible]ute procedural success, defined as AF termination, ≥10% slowing, or organization into [illegible]l tachycar[illegible].

RESULTS A total of 113 patients we[illegible]ed at 3 centers; 29 in group 1 and 42 each in groups 2 and 3. Group 1 enrollment was terminated early for futility. Foca[illegible]rivers o[illegible]e detected in all group 1 and 2 patients. Procedure time was significantly shorter in group 3 versus gro[illegible]s 1 a[illegible]2 ($p < 0.001$). In groups 1 and 2, acute success after rotor-only ablation was achieved in 12 patients (41%) and 11 (26[illegible]espectively. After 12 ± 7 months' follow-up, 4 patients (14%), 22 (52.4%), and 32 (76%) in groups 1, [illegible] respectiv[illegible] were AF/atrial tachycardia–free while off antiarrhythmic drugs (log-rank $p < 0.0001$). Grou[illegible]s patien[illegible]experience[illegible]igher success compared with groups 1 ($p < 0.001$) and 2 ($p = 0.02$).

CONCLUSIONS Outc[illegible]w[illegible]e poor with rotor-only ablation. PVAI + rotor ablation had significantly longer procedure time and lower e[illegible]acy than [illegible] + posterior wall + non-PV trigger-ablation. (Outcome of Different Ablation Strategies in Persistent and [illegible]ong-Standing Pers[illegible]t Atrial Fibrillation [OASIS]; NCT02533843) (J Am Coll Cardiol 2016;68:274–82) © 2016 by [illegible]e A[illegible]ican College of Cardiology Foundation.

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The low efficacy of medical therapy in maintaining sinus rhythm and the plethora of side effects associated with those drugs have prompted the search for new techniques and technologies to optimize the catheter ablation procedure for the treatment of atrial fibrillation (AF) (1).

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Pulmonary vein antrum isolation (PVAI) is still the cornerstone for AF ablation in paroxysmal AF patients, with reported success rates as high as 80% (2). However in persistent atrial fibrillation (PeAF) and long-standing persistent atrial fibrillation (LSPAF), the success rate is much lower even with repeat procedures (3). A potential reason behind this poor outcome is lack of information on the optimal ablation technique and the best targets to achieve freedom from arrhythmia (4). PeAF and LSPAF are chronic diseases associated with progressive atrial fibrosis and evolving pulmonary and nonpulmonary vein (non-PV) triggers (2). It is unclear whether substrate ablation alone, the elimination of triggers of AF, or a combination of both is the ideal ablation approach in this subset of AF population (4). This uncertainty is compounded by findings from the recently completed STAR-AF II (Substrate and Trigger Ablation for Reduction of Atrial Fibrillation II) trial, which failed to observe any reduction in the rate of recurrent AF when additional linear ablation or ablation of complex fractionated electrograms were performed along with PVI in PeAF patients (5). Of the many emerging approaches to modify AF-sustaining substrate, a promising strategy is the focal impulse and rotor modulation (FIRM)-guided ablation that targets electrical rotors and focal sources that are believed to be responsible for perpetuation of AF (6,7). Some trials have reported improved success rate with rotor ablation alone or in combination with PVAI versus PVAI alone, but none of these studies were randomized (7-9). We designed a prospective study, OASIS (Outcome of Different Ablation Strategies in Persistent and Long-Standing Persistent Atrial Fibrillation), to compare the efficacy of FIRM ablation with or without PVAI versus PVAI plus non-PV trigger ablation in PeAF and LSPAF patients.

METHODS

TRIAL DESIGN. OASIS was a nonblinded randomized trial comparing effectiveness of 3 ablation approaches for the treatment of AF. Consenting eligible subjects were randomly assigned (1:1:1) to undergo FIRM-guided ablation (group 1), FIRM+PVAI ablation (group 2), or ablation with PVAI, posterior wall (PW), and non-PV triggers (group 3) (Figure 1). The study protocol was approved by the institutional review boards of the respective institutions. The trial was conducted in accordance with the Declaration of Helsinki. The trial was registered at ClinicalTrials.gov (NCT02533843).

STUDY POPULATION. All patients presenting at the 3 participating centers (Texas Cardiac Arrhythmia Institute, Austin, Texas; Lexington Cardiology at Central Baptist, Lexington, Kentucky; and Cardiovascular Center, Bad Neustadt, Germany) with nonparoxysmal AF undergoing catheter ablation were screened. Patients were included in the study if they were ≥18 years of age, had PeAF or LSPAF, were undergoing their first ablation procedure, and were willing to provide written informed consent. Exclusion criteria included reversible causes of atrial arrhythmia (such as hyperthyroidism, pneumonia, pulmonary embolism, pericarditis, and excessive alcohol consumption), previous ablation procedures, and pregnancy.

RANDOMIZATION. A central computerized randomization scheme was generated using block randomization, and 3 randomly selected blocks were provided to the investigating sites. To maintain allocation concealment, the site administrators were instructed not to reveal the arm assignment until the subject's eligibility was verified and the subject was ready to be randomized.

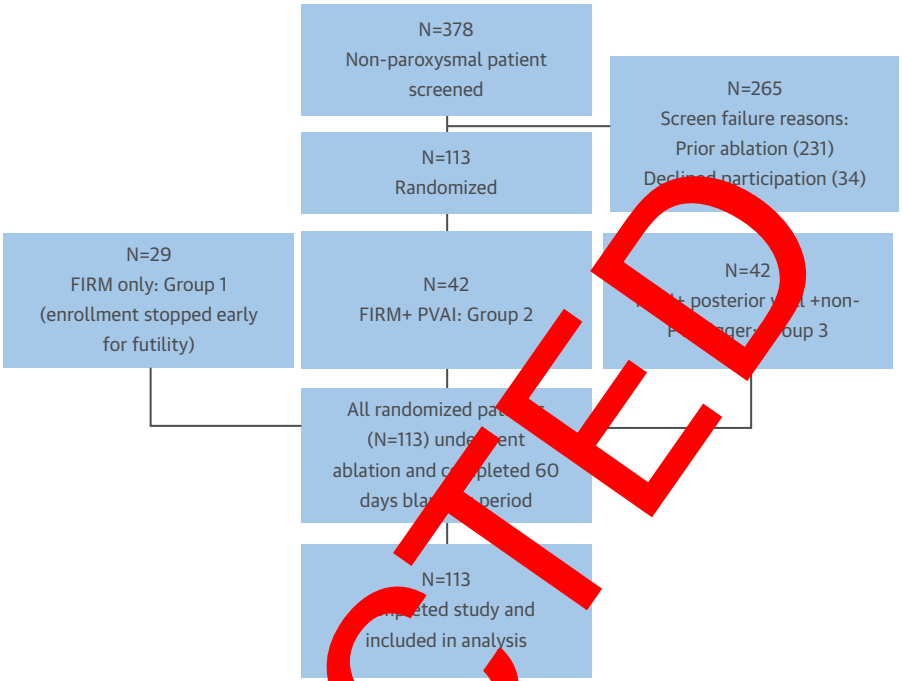
ENDPOINT. The primary endpoint was single procedure freedom from any recurrent AF/atrial flutter/atrial tachycardia (AT) while off antiarrhythmic drugs. Recurrence was defined as atrial arrhythmia (AF, atrial flutter, or AT) of >30 s duration while off antiarrhythmic drugs at follow-up. Any episodes that occurred during the first 60 days (blanking period) after the procedure were not considered a recurrence. Secondary endpoints included acute procedural success and periprocedural complications. Acute procedural success was defined as AF termination, ≥10% slowing, or organization into AT.

DEFINITIONS. Electrical rotors were defined as sustained clockwise or counterclockwise activation around a core (6,8). Focal impulses were centrifugal activation from an origin (8). Non-PV triggers were ectopic triggers originating from sites other than PV, such as interatrial septum, superior vena cava, left atrial appendage (LAA), crista terminalis, and coronary sinus. Both sustained (>30 s) and nonsustained triggers, including repetitive short-lasting bursts of arrhythmia (<30 s) or premature atrial

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation
AT = atrial tachycardia
CI = confidence interval
FIRM = focal impulse and rotor modulation
HR = hazard ratio
LAA = left atrial appendage
LSPAF = long-standing persistent atrial fibrillation
non-PV = nonpulmonary vein
PeAF = persistent atrial fibrillation
PVAI = pulmonary vein antrum isolation
PW = posterior wall
RF = radiofrequency

FIGURE 1 Patient Distribution Flowchart



Flowchart showing patient distribution according to eligibili ignment ablation strategy, and follow-up. FIRM = focal impulse and rotor modulation; non-PV = nonpulmonary vein; PVAI = pulmonary ve m isolation.

contractions ≥10 beats/min with earl activation from non-PV sites were t for abla n (10).

Acute procedural ccess as defin as AF termination, ≥10% s wing, o rga tion into AT (Online Figures 1A to 1

ABLATION PRO EDURE. Ou apping and ablation procedures h been described detail in earlier publication 6,11, Briefly, antiarrhythmic drugs, except amiodarone, w discontinued 3 to 5 days before e procedure; ami darone was stopped at least to 6 months prior to the ablation. All patients un rwent ation under general anesthesia and uni up d antico ulation with warfarin or novel oral anti gulant PVAI was always preceded by ablatio oup 2.

FIR PPING. Ablation commenced with FIRM m pping (1 ,12) in groups 1 and 2 patients. A dimensional map of the atria was constructed using an ctroanatomic mapping system (CARTO, Biosense Webster, Diamond Bar, California, or EnSite NavX, St. Jude Medical, St. Paul, Minnesota) before advancing the 64-pole basket mapping catheter (FIRMap, Abbott, Chicago, Illinois) in the right atrium first, followed by the left atrium next. FIRM mapping was performed during AF. Unipolar electrograms were recorded for 1 min and exported to a dedicated proprietary mapping system (RhythmView, Abbott, Abbott Park, Illinois). Radiofrequency (RF) energy was delivered with a 3.5-mm irrigated-tip ablation catheter, with the acute endpoint of AF source elimination as confirmed with FIRM remapping. Rotors and focal impulses were considered AF sources only if they lay in reproducible spatial regions with source precision. If AF persisted despite elimination of all rotors or converted into AT, the patient was cardioverted.

PVAI, PW, AND NON-PV TRIGGER ABLATION. The ablation procedure has been described in earlier publications from our group (11,12). Briefly, PVAI and electrical isolation of the LA PW were performed using 3.5-mm irrigated-tip catheter guided by circular mapping catheter, intracardiac echocardiography, and a 3-dimensional mapping system. RF energy was delivered with a maximum temperature setting of 42°C and a power of up to 45 W. An esophageal probe was utilized in all patients to monitor esophageal luminal temperature during ablation in areas in close proximity to the esophagus, such as the LA PW. When ablating the PW, the power was decreased to 35 W.

Complete abolition of all PV potentials rather than decrease in the amplitudes was the endpoint and was confirmed by entrance block. If ablation was unsuccessful in terminating the arrhythmia, cardioversion was performed to restore sinus rhythm.

After stable sinus rhythm was achieved either during ablation or after cardioversion, isoproterenol 20 to 30 μg/min for 15 to 20 min was given to disclose any non-PV triggers and to look for acute PV reconnection. Mapping was done using the circular mapping catheter during isoproterenol challenge to identify the site of origin of significant ectopic activity by comparing the activation sequence of the sinus beat with that of the ectopic beat. Additional RF energy was used to ablate the non-PV foci, both sustained and nonsustained. Patients were discharged after an overnight stay on their previously ineffective antiarrhythmic drugs, with the exception of amiodarone, which was never restarted during the 2-month blanking period.

FOLLOW-UP. Follow-up was performed at 1, 3, 6, and 12 months with office visits, cardiology evaluation, 12-lead electrocardiogram, and 7-day Holter monitoring at 3, 6, and 12 months. Additionally, patients were given event recorders for the first 5 months following the procedure and were asked to transmit their rhythm every time they had symptom compatible with arrhythmias and at least 3 times week even if asymptomatic.

Oral anticoagulant therapy was continued up to 6 months following the procedure, after which it was discontinued in all patients that remained arrhythmia-free. If the patients underwent isolation, a transesophageal echocardiography was performed at 6 months to assess the contractility and flow velocity of the LAA. In case of inadequate velocity, patients were kept on anticoagulants (13).

SAMPLE SIZE. In the absence of historical data on FIRM-guided ablation procedure in nonparoxysmal AF population, we were not able to perform a formal power analysis. Instead, consecutive patients were approached until we had enrolled 42 patients in each group. The justification for this sample size was based on feasibility of enrolling enough participants within a reasonable time frame.

A relatively high recurrence among the FIRM-only subjects (group 1) triggered an unplanned interim assessment by the internal safety committee. The committee recommended terminating the arm for futility and continuing with the planned enrollment for other 2 groups. The results of the FIRM-only ablation (group 1) have been recently published by our group (6).

STATISTICAL ANALYSIS. The primary analysis was conducted for the intent-to-treat population, which consisted of all randomized patients undergoing ablation procedure. Primary endpoint was tested using survival analysis method, and the null hypothesis was tested using log-rank test. Multiple-comparison adjustment of survival curves was performed using Tukey-Kramer method. Subjects who were recurrence-free at the end of follow-up were censored. AF-free time was defined as time from procedure date to censor date. Survival curves were constructed using Kaplan-Meier method. Unadjusted and multivariable-adjusted Cox regression models were used for assessing independent predictors of AF-free survival. Sex and AF type were entered into the model as covariates. Incidence of procedural complications was compared between cohorts using Fisher exact test. Patient demographic and clinical characteristics were reported using descriptive statistics. Continuous data were described as mean ± SD and as counts and percentages if categorical. Analysis of variance and chi-square tests were used to compare groups. Tukey-Kramer method was used for analysis of variance post hoc pairwise comparison. Procedure time and radiofrequency time were compared between groups 2 and 3 by using independent samples Student *t*-test.

All tests were 2-sided, and a p value of <0.05 was considered statistically significant. Analyses were performed using SAS software (version 9.2, SAS Institute Inc., Cary, North Carolina).

RESULTS

STUDY POPULATION. A total of 378 patients were screened during the study period and 113 were enrolled at the 3 centers; 29 in group 1 and 42 each in groups 2 and 3. Enrollment in group 1 was terminated early for futility after enrollment of the 29 patients. Study design and patient disposition are presented in a flow diagram (**Figure 1**). Groups were well balanced on baseline and clinical characteristics (**Table 1**). In summary, for groups 1, 2, and 3, respectively, LSPAF was present in 31%, 29%, and 31%; LA diameter was 4.73 ± 0.75, 4.84 ± 0.74, and 4.67 ± 0.69; and left ventricular ejection fraction was 54.5 ± 9.9, 55.4 ± 9.9, and 55.4 ± 9.5.

ELECTRICAL ROTORS. Focal drivers or rotors were detected in all group 1 and 2 patients with a mean of 4.0 ± 1.2 and 4.2 ± 1.7 rotors per patient, respectively ($p = 0.55$). A total of 116 AF rotors (61% LA and 39% right atrium) and 177 (67% LA and 33% right atrium) lying in widespread locations were detected in groups

TABLE 1 Baseline Demographic and Clinical Characteristics

	Group 1 (n = 29)	Group 2 (n = 42)	Group 3 (n = 42)	p Value
Age, yrs	62.4 ± 10.3	65.1 ± 10.2	67.6 ± 8.5	0.08
AF type				
Persistent	20 (69.0)	30 (71.4)	29 (69.1)	0.97
LSPAF	9 (31.0)	12 (28.6)	13 (31.0)	
Male	23 (79.3)	28 (66.7)	29 (69.1)	0.49
Body mass index, kg/m^2	31.1 ± 4.4	32.8 ± 7.1	32.9 ± 7.6	0.51
Left atrial diameter, cm	4.73 ± 0.75	4.84 ± 0.74	4.67 ± 0.69	0.62
Left ventricular ejection fraction, %	54.5 ± 9.9	55.4 ± 9.9	55.4 ± 9.5	0.93
Hypertension	25 (86.2)	31 (73.8)	27 (64.3)	0.12
Diabetes	4 (13.8)	6 (14.3)	8 (19.1)	0.78
Obstructive sleep apnea	7 (24.1)	7 (16.7)	9 (21.4)	0.73
Congestive heart failure	6 (20.7)	8 (19.1)	6 (14.3)	0.75
Stroke/transient ischemic attack	2 (6.9)	2 (4.8)	2 (4.8)	1.00

Values are mean ± SD or n (%).
AF = atrial fibrillation; LSPAF = long-standing persistent atrial fibrillation.

1 and 2, respectively. Distribution of AF rotors in the 2 groups is summarized in Table 2 and Figure 2.

NON-PV TRIGGERS. During the isoproterenol challenge, non-PV triggers were detected in a[illegible] patients in group 3. The foci were most commonly mapped to the coronary sinus (73.8%), LAA (38.1%), interatrial septum (50.0%), superior vena cava (28.6%), and mitral valve annulus (4.8%). The sources were ablated.

Procedure time was 222 ± 49, 233 ± 48, and 131 ± 51 min in groups 1, 2, and 3, respectively (p < 0.001); it was significantly shorter in group 3 than in groups 1 and 2 (p < 0.001). Compared with group 2, group 3 patients had significantly longer RF time (42.3 ± 14.1 min and 54.1 ± 21.4 min, respectively; p = 0.003). Procedural parameters are summarized in Table 2. After rotor ablation, acute success was achieved in 12 patients (41%) and 11 (26%) in groups 1 and 2, respectively.

FREEDOM FROM ARRHYTHMIA RECURRENCE. After 12 ± 7 months' follow-up, 4 of 29 patients (14%) in group 1, 22 (52.4%) in group 2, and 32 (76%) in group 3 were AF-/AT-free without antiarrhythmic drugs (log-rank p < 0.0001). Patients in group 3 experienced significantly higher success compared with patients in groups 1 (p < 0.001) and 2 (p = 0.02) (log-rank p adjusted for multiple pairwise testing). Sensitivity analysis of the primary endpoint was performed after stratifying by AF type. In PeAF patients, the success rate was 53% (16 of 30) and 78% (21 of 29) in groups 2 and 3, respectively (log-rank p = 0.13). In the LSPAF cohort, 6 of 12 patients (50.0%) in group 2 and 11 of 13 (84.6%) in group 3 were recurrence-free (log-rank p = 0.06).

PREDICTOR OF RECURRENCE. We assessed the prognostic role of the ablation approach by fitting a Cox model. Group 1 was excluded from this analysis. These findings revealed that compared with group 3 (PVAI, PW, and non-PV trigger ablation), group 2 (FIRM+PVAI ablation) was associated with significantly higher risk of recurrence. Unadjusted hazard ratio (HR) was 2.37 (95% confidence interval [CI]: 1.1 to 5.07); p = 0.025. After adjusting for sex and AF type the in multivariable model the hazard ratio was 2.36 (95% CI: 1.11 to 5.09; p = 0.027).

COMPLICATIONS. No procedure-related adverse events occurred in any of the patients in group 1. Two patients (1 in group 2 and 1 in group 3) had minor groin hematomas and 1 patient in group 2 had a small pericardial effusion that was conservatively managed with fresh-frozen plasma and protamine. No major adverse events such as stroke, pulmonary stenosis, esophageal injury, or major bleeding events were reported.

TABLE 2 Procedural Characteristics of the Study Population (n = 113)

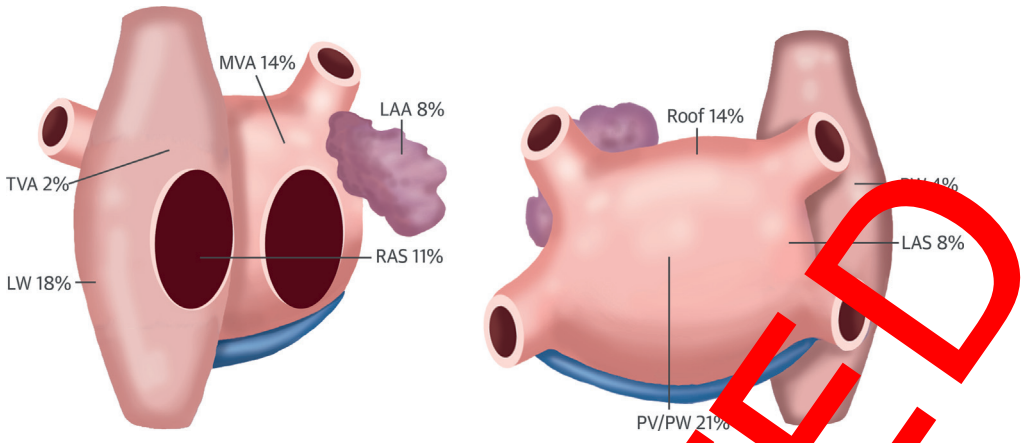
	Group 1 (n = 29)	Group 2 (n = 42)	Group 3 (n = 42)	p Value
Procedural time, min	222 ± 49	233 ± 48	131 ± 51	<0.001
Fluoroscopy time, min	16.8	21.1	29.0 ±15.8	<0.001
Radiofrequency time, min	16	42.3 ± 14.1	54.1 ± 21.4	<0.001
Direct current cardioversion	29 (100)	38 (90.5)	31 (73.8)	0.004
Number of rotors	116	177	NA	
RA rotors	8)	59 (33.3)	NA	0.34
LA rotors	71 (61.2)	118 (66.7)		
Rotors per patient	4.0 ± 1.2	4.21 ± 1.70	NA	0.55
RA rotors	1.55 ± 0.95	1.41 ± 1.01	NA	0.54
LA rotors	2.45 ± 1.06	2.81 ± 1.19	NA	0.19
Complications	0 (0.0)	2 (4.8)	1 (2.4)	0.63

Values are mean ± SD or n (%) unless otherwise indicated.
LA = left atrium; NA = not available; RA = right atrium.

DISCUSSION

To the best of our knowledge, this is the first randomized trial that compared the efficacy of FIRM ablation with or without PVAI versus PVAI + PW + non-PV trigger ablation in PeAF and LSPAF patients (Central Illustration). Our main findings were the following: 1) acute procedural success after targeting the FIRM-identified rotors was achieved in a small number of patients—41% and 26% in group 1 and 2, respectively; 2) rotor-only ablation had very poor outcome in terms of arrhythmia recurrence for which that arm was terminated prematurely; and 3) PVAI plus rotor ablation had significantly longer procedure time and lower efficacy than PVAI + PW + non-PV trigger ablation.

FIGURE 2 Distribution of the Rotors in the Atria



Distribution of the rotors in the left atrium and the right atrium. LAA = area around the left a[illegible] appendage; LAS = [illegible]ial septum; LW = lateral wall; MVA = area around the mitral valve annulus; TVA = area around the tricuspid va[illegible]lus; PV = pulmonary [illegible]eins; PW = posterior wall; RAS = right atrial septum.

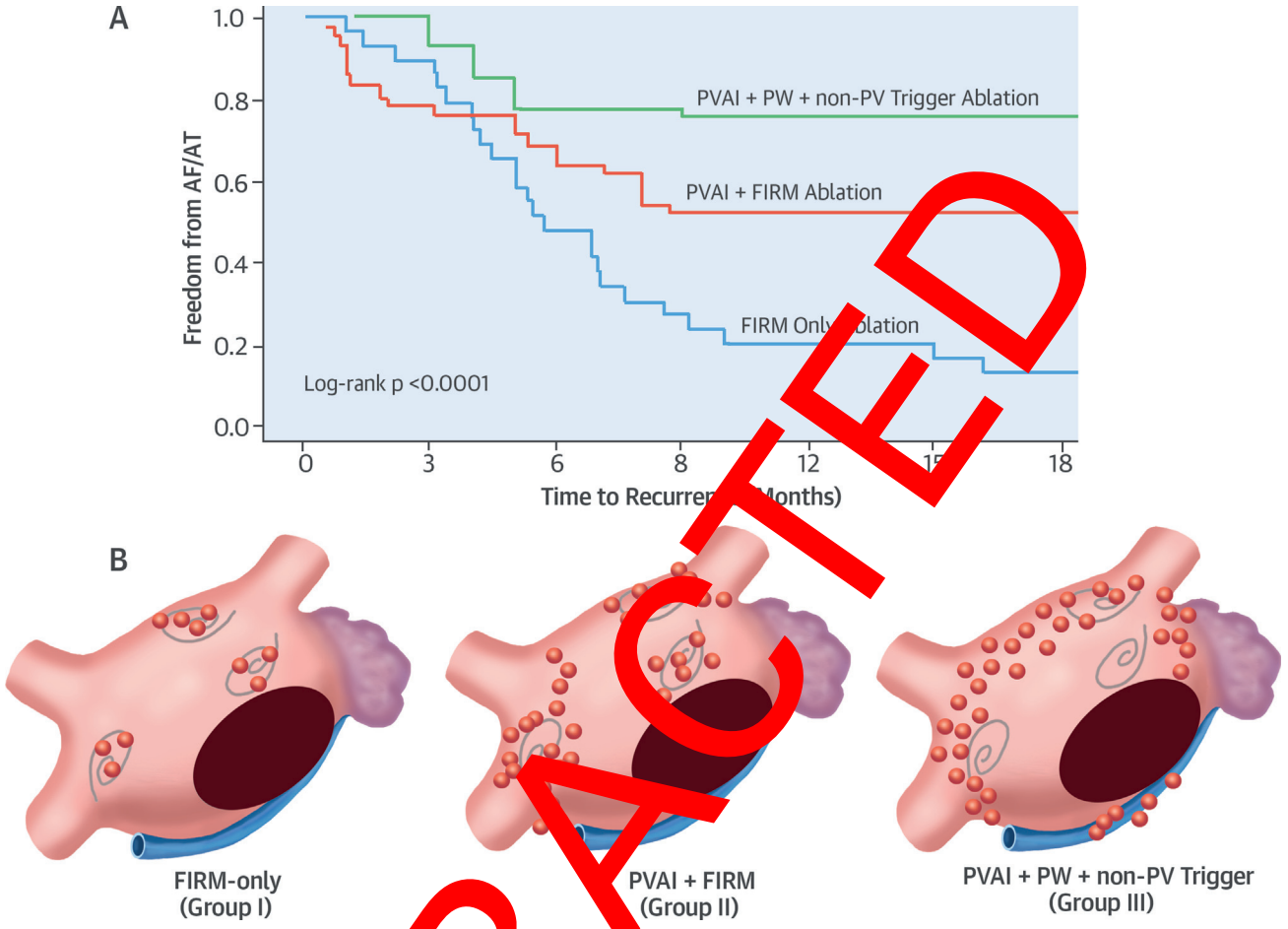
We observed a significantly longer procedure time with rotor ablation with or without PVAI in our study population, which was in agreement with some earlier trials (7,14) and in disparity with others (15). This discrepancy can be due to detection of mo[illegible] rotors than that reported by the CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) study (mean of 4 vs. 2 per patient) that most likely mad[illegible]e p[illegible]cedure time longer (15).

Despite lengthier procedure time, [illegible] fail[illegible] to accomplish the high acute success [illegible]h rot[illegible]lation as reported by earlier studies (15-17), a po[illegible]le explanation for which is the d[illegible]nce in the study population. In all of the ab[illegible]-men[illegible]ed trials, the population was composed of subjects [illegible]h paroxysmal and persistent AF, whereas our study included only nonparoxysmal A[illegible] (PeAF a[illegible]d LSPAF) patients. It is well known that [illegible]te ter[illegible]nation is not an easy task to accomplish in [illegible]bset of [illegible]F population (18). In accorda[illegible] with [illegible] fin[illegible]gs, 2 recently published sin[illegible]-ce[illegible]er experie[illegible]s (7,19), have reported sim[illegible]rly lo[illegible]e procedural success in nonparoxy[illegible]l po[illegible]lation. [illegible]ther feasible reasons might be the sm[illegible]ample size, nonrandomized study design with possibl[illegible]s in patient selection, and the learning-curve effect (6).

In our study, acute success was achieved in higher numbers of patients in group 1 than in group 2. However, no conclusions can be drawn from this observation, as the groups were unbalanced in term[illegible] of number of [illegible]tients included in the analysis. At 12[illegible]7 months' [illegible]llow-up, only 14% of our patients t[illegible]under[illegible]nt rotor-only ablation (group 1) remained arrhythmia-free while off antiarrhythmic [illegible]. Because of this poor outcome, this arm was deem[illegible] futile and discontinued prematurely to avoid exp[illegible]ing the patients to inappropriate risks. Our s[illegible]cess rate was surprisingly lower than the reported res[illegible]ts of Miller et al. (9) (71.4%) and the CONFIRM trial (70.6%) (15), which can again be due to the difference in the selected population. It is also possible that ablation limited to only rotors is not sufficient to maintain sinus rhythm in nonparoxysmal AF and additional ablations are required. This was evidenced by the procedure outcome in groups 2 and 3 of our study patients, whereas additional ablations led to a better success rate compared with that of group 1; after 12 ± 7 months' follow-up, the single-procedure success rate while off antiarrhythmic drugs was 4 (14%), 22 (52.4%), and 32 (76%) in groups 1, 2, and 3, respectively ($p < 0.0001$). Although the arrhythmia-free survival following PVAI + rotor ablation (group 2) in our population was lower than that of previous studies (Miller et al. (9) 80.5% and CONFIRM (15) 82.4%), it was comparable with the findings of Tomassoni et al. (19) (single procedure while off antiarrhythmic drugs success rates: 58% in PeAF; and 25% in LSPAF).

Our results demonstrated the extensive approach of PVAI + LA PW + ablation of non-PV triggers to be the most effective ablation strategy in the

CENTRAL ILLUSTRATION **Impact of Rotor Ablation in Nonparoxysmal AF Patients**



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(A) Kaplan-Meier curve comparing freedom from recurrence across the study groups. After 12 ± 7 months' follow-up, 4 patients (14.0%), 22 (52.4%), and 32 (76.0%) in groups 1, 2, and 3, respectively, were atrial fibrillation (AF)/atrial tachycardia (AT)-free while off antiarrhythmic drugs (log-rank p < 0.0001). Any episodes that occurred during the first 60 days (blanking period) after the procedure were not considered a recurrence. **(B)** The 3 groups based on the ablation strategies. FIRM = focal impulse and rotor modulation; non-PV = non-pulmonary vein; PVAI = pulmonary vein antrum isolation; PW = posterior wall.

nonparoxysmal AF population. Several factors may have concertedly contributed to the observed high success rate of this ablation approach such as isolation of LA PW and ablation of non-PV triggers detectable by isoproterenol challenge.

The common embryologic origin of the PV and the LA PW provides the anatomic basis that suggests the role of LA PW as an arrhythmogenic substrate in the origin and maintenance of AF. Consequently, isolation of the LA PW has been shown to increase the short- and mid-term success rate of PVAI in nonparoxysmal AF patients (20–23). With the persistence of AF, both the frequency and number of non-PV triggers increase and several studies have shown the benefits of ablation of those extra-PV foci in providing effective and durable arrhythmia-free survival (2,24–27).

We observed the best outcome with substrate ablation including non-PV triggers combined with PVAI in nonparoxysmal AF patients, reaffirming the current guideline recommendation that patients with PeAF undergoing catheter ablation should receive additional substrate ablation to improve outcome (28). However, in the recently published STAR-AF-II trial, no reduction in recurrence was observed with additional substrate ablation such as linear ablations or ablation of complex fractionated electrograms (5). The discrepancy can be best explained by quoting the

STAR-AF-II investigators: "Perhaps neither complex electrograms nor lines are the correct supplemental targets for ablation." Several earlier randomized trials have reported no additional advantages of linear ablation approach over PV isolation alone in AF/AT patients although the lines required significantly more ablation time, greater radiation doses, and longer procedure duration (29–31). Similarly, complex fractionated electrogram ablation has been reported to confer no long-term incremental benefit when performed in addition to PVAI (32,33).

Last but not least, although more extensive ablation was performed in group 3, it took less procedure and fluoroscopic time than the other 2 strategies while offering comparable safety and better efficacy.

STUDY LIMITATIONS. AF recurrence could have been underestimated as the patients were not constantly monitored, and we could have also missed some asymptomatic events. However, patients included in this study were symptomatic and were able to distinguish their AF symptoms. Also, in an earlier study conducted by our group, we did not observe significant differences in the captured arrhythmia events between the implantable loop recorder and conventional monitoring (34). A lengthier follow-up would have provided a better comparison of the long-term outcome of PVAI + rotors ablation versus PVAI + LA PW + non-PV triggers ablation, but historically, the success rate of the latter ablation approach has been similar after ≥2 years' follow-up (27). Finally, the sample size is relatively small. However, we could still detect a true effect that is statistically significant.

CONCLUSIONS

This is the first randomized study comparing 3 ablation strategies in nonparoxysmal AF patients and reporting a very poor outcome with rotor-only ablation. Furthermore, acute procedural success was achieved in very few after the ablation of rotors. Additionally, rotor ablation combined with PV isolation had significantly longer procedure time and lower efficacy than the ablation strategy including isolation of LA PW and non-PV triggers along with PV isolation in patients with PeAF or LSPAF.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: In patients with nonparoxysmal (persistent and long-standing persistent) AF, ablation of focal impulses and electrical rotors alone or in combination with isolation of the PV does not generally promote durable arrhythmia-free survival; targeting of non-PV triggers is also necessary to enhance procedural success.

TRANSLATIONAL OUTLOOK: Further studies are needed to define systematic approaches for identification and ablation of arrhythmogenic loci in patients with nonparoxysmal AF and to compare the efficacy and safety of alternative strategies in adequately powered randomized trials.

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KEY WORDS FIRM-guided ablation, nonparoxysmal AF, non-PV triggers, PVAI, rotors

APPENDIX For supplemental figures, please see the online version of this article.

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