


ORIGINAL ARTICLE

Association with the nonparoxysmal atrial fibrillation duration and outcome of ExTRa Mapping-guided rotor ablation

Yusuke Okuyama MD¹  | Tomoya Ozawa MD, PhD¹ | Takuma Nishikawa MD¹ |
Yusuke Fujii MD, PhD¹ | Koichi Kato MD, PhD¹ | Yoshihisa Sugimoto MD, PhD^{1,2} |
Yoshihisa Nakagawa MD, PhD¹ | Takashi Ashihara MD, PhD^{1,2}

¹Department of Cardiovascular Medicine, Shiga University of Medical Science, Otsu, Japan

²Department of Medical Informatics and Biomedical Engineering, Shiga University of Medical Science, Otsu, Japan

Correspondence

Takashi Ashihara, Department of Medical Informatics and Biomedical Engineering, Shiga University of Medical Science, Seta Tsukinowa-cho, Otsu 520-2192, Shiga Prefecture, Japan.

Email: ash@belle.shiga-med.ac.jp

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Abstract

Background: Additional ablation strategies after pulmonary vein isolation (PVI) for patients with nonparoxysmal atrial fibrillation (non-PAF) lasting ≥ 2 years have not been fully effective. This is presumably because of insufficient identification of non-PAF maintenance mechanisms. In this study, we employed a novel online and real-time phase mapping system, ExTRa Mapping, to identify and modulate rotors as one of the non-PAF maintenance mechanisms in patients with non-PAF sustained after PVI. We investigated the relationship between outcomes of ExTRa Mapping-guided rotor ablation (ExTRa-ABL) and non-PAF duration prior to this procedure.

Methods: This study consisted of 73 non-PAF patients (63 ± 8 years, non-PAF duration 31 ± 37 months) who underwent the first ExTRa-ABL in patients with non-PAF sustained after completion of PVI.

Results: Freedom from non-PAF/atrial tachycardia (AT) recurrence at 12 months after ExTRa-ABL was achieved in 50 (69%) of patients. The non-PAF duration prior to ExTRa-ABL was significantly longer in patients with non-PAF/AT recurrence after ExTRa-ABL compared with those without (56 ± 50 vs. 19 ± 22 months, $p = .001$). In patients with non-PAF duration of ≤ 60 months prior to ExTRa-ABL, compared with > 60 months, non-PAF/AT-free rate was significantly higher (68.9% vs. 23.1%, $p < .001$), during the follow-up of 36 ± 18 months.

Conclusions: A non-PAF duration of ≤ 60 months prior to ExTRa-ABL was associated with a better outcome. The effect of ExTRa-ABL was considered to be limited in patients with > 60 months of non-PAF duration.

KEYWORDS

atrial fibrillation, catheter ablation, phase mapping, rotor, visualization

1 | INTRODUCTION

Pulmonary vein isolation (PVI) by catheter ablation for patients with atrial fibrillation (AF) has been established as one of the most

effective methods to eliminate triggers of paroxysmal AF (PAF).¹ However, there is less evidence supporting catheter ablation of nonparoxysmal AF (non-PAF). Indeed, the pathogenesis of non-PAF needed for catheter ablation remains uncovered despite advances in

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the ablation techniques. The difficulty in non-PAF ablation may be because of the unsolved mechanisms sustaining non-PAF. The clinical outcomes of extended non-PAF ablation strategies modifying regions where indirect indicators suggesting AF perpetuators, such as complex fractionated atrial electrograms and low voltage areas, in addition to the PVI, remain unsatisfying.²⁻⁴ As one of the alternative effective ablation strategies, rotor modulation by targeting direct indicators of non-PAF perpetuators has been proposed to control the AF persistency.^{5,6} However, previous rotor ablation strategies were not sufficiently able to improve the non-PAF ablation outcomes.^{7,8}

Based on the above, we hypothesized that a rotor ablation conducted with an accurate visualization of rotors would improve the ablation outcomes even in patients with non-PAF recurrence or without non-PAF termination after the completion of the PVI (residual non-PAF) with a long non-PAF duration. For a direct and precise visualization of non-PAF rotors, we developed an online and real-time phase mapping system (ExTRa Mapping™, Nihon Kohden Co.), which can visualize a voltage-dependent phase map like high-resolution optical mapping (Figure 1).⁹ To improve mapping accuracy, the ExTRa Mapping system incorporates a specialized artificial intelligence (AI) system that solves the optimization problem of spatiotemporal complement of intra-atrial bipolar signals. We preliminarily reported that catheter ablation with the use of this system was effective in reducing AF persistency.¹⁰

Thus, in this study we employed ExTRa Mapping system to detect and modulate rotors and investigated the relationship between outcomes of the ExTRa Mapping-guided rotor ablation (ExTRa-ABL) and the non-PAF duration prior to the first ExTRa-ABL in patients with residual non-PAF.

2 | METHODS

2.1 | Patient population

Out of consecutive 232 patients with non-PAF, who underwent catheter ablation from September 2015 to August 2020 at the Shiga University of Medical Science hospital, 73 who received the first ExTRa-ABL because of residual non-PAF were enrolled in this study. Even in the first ablation session for non-PAF, patients with ineffective internal cardioversion of non-PAF after completion of the PVI were also included. We excluded patients who had no sinus rhythm record prior to inclusion. Patients without ECG records at least once a year, for example at annual health check, were also excluded as unknown duration of non-PAF prior to the first ExTRa-ABL. Patients with thrombus detected in left atrial (LA) appendage by transesophageal echocardiograms, mitral regurgitation of grade ≥ 3 , PAF, and without consent to participate in this study were also excluded. This study complied with the principles of the Declaration of Helsinki.

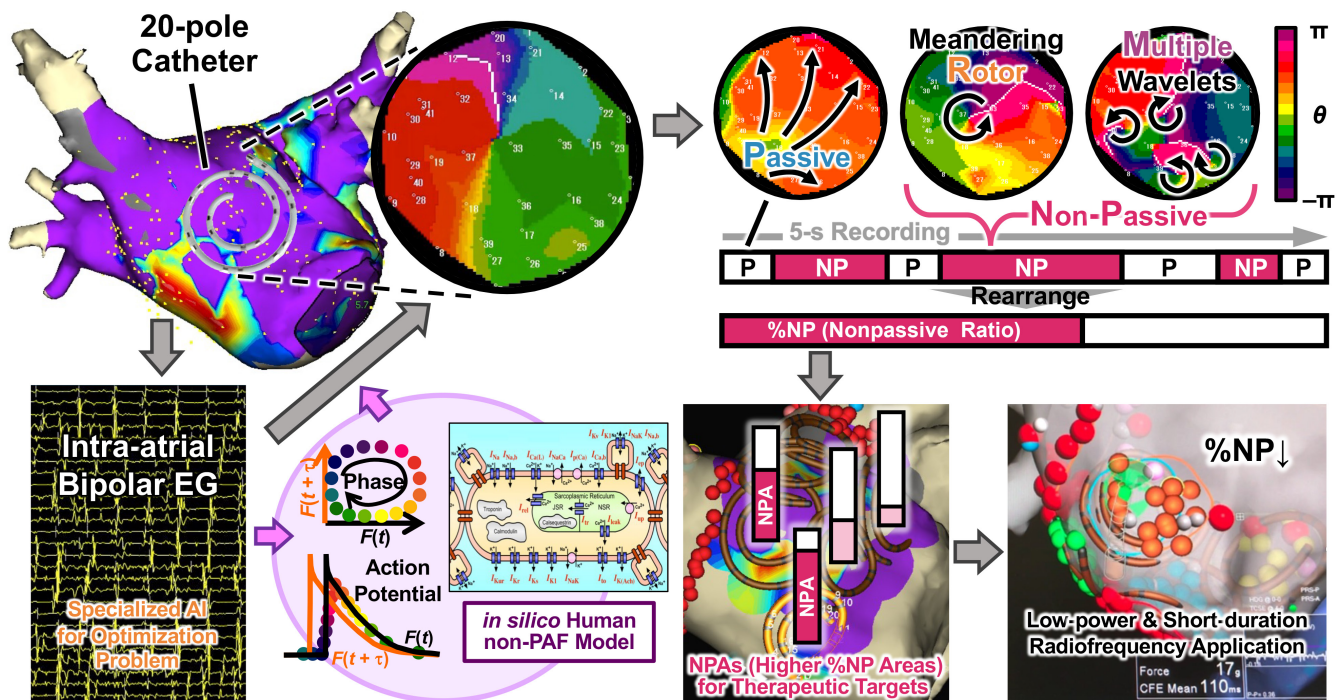


FIGURE 1 Our clinically available phase mapping system (ExTRa Mapping™) and the ablation procedure. Online and real-time imaging of the wave dynamics during AF was achieved by introducing a high-speed computation together with both an in silico analysis and artificial intelligence to resolve the optimization problem of the spatiotemporal interpolation of the intra-atrial bipolar signals. The AF rotors (nonpassive activations) were visualized as voltage-dependent phase map movies created in a few seconds. The low-power and short-duration radiofrequency ablation procedure was conducted targeting nonpassively activated areas (NPAs) where AF rotors were observed frequently.

Written informed consent for the ablation and participation in this study was obtained from all patients, and the protocol was approved by our institutional ethics committee on human research.

Non-PAF was defined according to the HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement as persistent AF (PersAF) or long-standing persistent AF (LS-PersAF).³ Non-PAF duration was calculated from the last sinus rhythm record in the best available ECG. Transthoracic and transesophageal echocardiograms were performed before each ablation to evaluate the left ventricular function, left atrial diameter, detect valvular diseases, and exclude the presence of thrombi. All antiarrhythmic drugs except amiodarone were discontinued for at least three half-lives before the ablation procedure. In some cases, amiodarone was temporarily employed to avoid both a rapid ventricular response during AF and post-termination pauses causing syncope.

2.2 | Ablation procedure with ExTRa mapping system

Firstly, a PVI with a 3D electroanatomic mapping system (EnSite NavX™, Abbott) was performed during AF in all patients under intravenous light sedation with dexmedetomidine and thiopental sodium. If there was a reconnection between the pulmonary veins and LA, the PVI was completed. In patients with sustained AF even after achievement of PVI, online and real-time phase mapping during AF with the ExTRa Mapping system was then performed on the entire LA, excluding the isolated pulmonary veins and their antral regions.

As shown in Figure 1, the rotor visualizations were based on 41 intra-atrial bipolar signals recorded by a 20-pole spiral-shaped multi-electrode catheter (2.5 cm in diameter). When the alignment of bipolar electrodes is orthogonal to the direction of excitation propagation, some signals can be lost. Moreover, far-field ventricular potentials overlap with atrial potentials and can interfere with the analyses of consecutive atrial potentials. To overcome these difficulties: the “lost bipolar signals” and “overwritten bipolar signals,” the specialized AI system equipped into the ExTRa Mapping system complements signals by in silico rapid prediction of the spatiotemporal atrial excitations based on the timing of surrounding signals. The accuracy of this AI has been confirmed through in silico evaluation and experimental optical mapping study.⁹ Phase map movies were automatically created within a few seconds based on a 5-s recording of the intra-atrial signals during AF.

The phase mapping of the entire LA with the ExTRa Mapping system took ≤ 20 min. Then AF rotors, in the forms of meandering rotors (R) and multiple wavelets (M), were detected as nonpassively activated areas (NPAs). Nonpassive rotational activations were defined in the given mapping area as R or M according to the excitation synchronization and the number of phase singularities (PSs), corresponding to the centers of the rotational activations. When the activations in the mapping area were poorly synchronized and there were one or two PSs, the rotor behavior judged as R, and when there were three or more PSs, judged as M. The ratio of the time that R

or M was observed to 5-s recording time was calculated as %R or %M, respectively. Then, the summation of them gave the ratio of the nonpassive activations (%NP). In each patient, the NPAs, therapeutic targets of the ExTRa-ABL, were determined by identifying areas with the top four to six highest %NP areas within the areas with %NP $> 50\%$ and referring to spatial continuity of the high %NP areas. The rationale for determining NPAs in this way was that, in our preliminary study, the top five (4.6 ± 1.1) highest %NP areas contained $> 70\%$ of the whole nonpassive rotational activations in each patient and were the most efficient at capturing rotors relative to the number of mapped areas. In the present study, to assess the complexity of excitation wave dynamics of rotors, ratio of %M to %NP (%M/%NP) was evaluated.

To modulate NPAs, low-power and short-duration radiofrequency application with 20–25 watts of output was done. Radiofrequency applied for 5–10 s for each ablation point, using a 3.5 mm-tip irrigated catheter (FlexAbility™, Abbott) with a dragging technique filling the NPA. The endpoint of the ExTRa-ABL was the sufficient modulation of the rotor behaviors. To assess the rotor modulation, remapping with the system and evaluating the decrease in the %NP value with absolute difference ≥ 15 was conducted just after modulating NPAs. If the %NP value insufficiently decreased, additional modulation of NPA was performed, and the %NP values were reconfirmed. All ExTRa-ABL procedures including remapping by the system were performed within 40 min by one operator to avoid any inter-operator difference. Internal cardioversion was performed only at the end of the session if AF was sustained even after ExTRa-ABL.

2.3 | Evaluated endpoints and follow-up regimen

The patients were followed at 1, 3, and 6 months and every year after the procedure. A standard resting 12-lead ECG and several weeks of event ECGs were monitored. We set the primary endpoint as the recurrence of non-PAF and/or the occurrence of sustained AT (non-PAF/AT recurrence), excluding PAF and paroxysmal AT, because the ExTRa-ABL aimed to modify the AF maintenance mechanisms (rotors) rather than AF initiation mechanisms (triggers), to evaluate the effect on non-PAF rotors. In addition, any recurrent atrial tachyarrhythmias were set as the secondary endpoint as a substantial clinical outcome. The rate of freedom from each endpoint for 12 months after ExTRa-ABL and the long-term outcome after the first ExTRa-ABL were evaluated with a mean follow-up period of 36 months. Recurrence of atrial tachyarrhythmias was defined as existence of AF and/or AT of more than 30 s. The recurrent modes of atrial tachyarrhythmias were defined according to the HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement.³

2.4 | Statistical analyses

All continuous variables were expressed as the mean \pm SD. An unpaired t-test was used to compare the unpaired variables between

the patient groups. A chi-squared test or Fisher exact test was used to compare the categorical variables between the patient groups. In addition, the freedom from the primary and secondary endpoints was estimated by the Kaplan–Meier analysis, and time-to-event analyses were performed using the log-rank test. A *p*-value of <.05 was considered statistically significant.

3 | RESULTS

3.1 | Patient characteristics

During the study period, ExTRa-ABL was performed in 73 residual non-PAF patients. The mean age was 63 ± 8 years, and the majority of the patients were male (78.1%). Furthermore, 41 patients (56.2%) had LS-PersAF. The number of previous conventional ablation before the first ExTRa-ABL was 1.6 ± 0.7 per patient, and the mean CHA₂DS₂-VASc score was 2.1 ± 1.4 . Further patient characteristics are given in Table 1. After ExTRa-ABL, 50 mg of pilsicainide or 100 mg of flecainide per day was taken as needed in only two patients with symptomatic PAF and/or PAT. Amiodarone 96 ± 13 mg per day was prescribed only in 14 (19.2%) patients after the 3 months of blanking period following ExTRa-ABL, and efforts were made to discontinue it as soon as possible. Indeed, 10 (71%) of those patients discontinued taking amiodarone within 2 years. The details are given in Table S1.

After confirming the completion of PVI, phase mapping of the entire LA with the ExTRa Mapping system was accomplished except for the regions isolated by prior ablation procedures. Mean %NP, %R, %M, and %M/%NP were 62 ± 12 , 39 ± 10 , 24 ± 10 , and 0.38 ± 0.13 , respectively (Table 1). Comparing between patients in ≤ 60 M and > 60 M groups, there was no statistical difference in both mean %M/%NP (0.37 ± 0.14 vs. 0.39 ± 0.11 , *p* = .27) and the ratio of non-PAF recurrence (0.37 ± 0.14 vs. 0.39 ± 0.12 , *p* = .20). Non-PAF duration also showed no correlation with %M/%NP (*R* = .09, *p* = .11). Internal cardioversion with 10–20 J biphasic shock was performed at the end of the ExTRa-ABL in all patients except for in four (5%) patients with direct AF termination only by ExTRa-ABL. No procedural complications during the ablation occurred except for one cardiac tamponade (Table 2).

3.2 | Follow-up at 12 months after rotor ablation

The follow-up data after the 3-month blanking period were available from all 73 patients with a mean follow-up period of 36 ± 18 months (range 12–69 months, median 36 months) (Table 1). There was no statistical difference in the follow-up period between the groups with and without recurrence (33 ± 14 vs. 37 ± 19 months, *p* = .29). One patient died of a stroke 28 months after the first ExTRa-ABL because of self-discontinuation of taking oral anticoagulants (Table 2).

As shown in Figure 2, 12 months after the first ExTRa-ABL, 50 of 73 (69%) patients were free from the primary endpoint of the non-PAF/AT. Of the 23 patients with recurrence, 19 had recurrence of non-PAF and four had that of sustained AT. For the secondary

TABLE 1 Patient characteristics at baseline.

Patient characteristics	N = 73
Male, <i>n</i> (%)	57 (78.1)
Long-standing persistent AF, <i>n</i> (%)	41 (56.2)
Age, year	63 ± 8
BMI	24.5 ± 3.6
Non-PAF duration, months	31 ± 37
Time since diagnosis, months	68 ± 83
Follow-up period, months	36 ± 18
No. of prior PVI	1.6 ± 0.7
ExTRa-ABL in index procedure, <i>n</i> (%)	42 (57.5)
BNP, pg/mL	168.7 ± 136.1
Number of NPAs, <i>n</i>	4.3 ± 1.3
%NP	62 ± 12
%R	39 ± 10
%M	24 ± 10
%M/%NP	0.38 ± 0.13
TTE parameters	
LVEF, %	56 ± 8
LA diameter, mm	44 ± 6
Comorbid conditions	
CHA ₂ DS ₂ -VASc score	2.1 ± 1.4
CHADS ₂ score	1.3 ± 1.0
Hypertension, <i>n</i> (%)	49 (67.1)
Diabetes mellitus, <i>n</i> (%)	16 (21.9)
Stroke, <i>n</i> (%)	6 (8.2)
Heart failure, <i>n</i> (%)	10 (13.7)
Vascular disease, <i>n</i> (%)	4 (5.5)
Mitral regurgitation, <i>n</i> (%)	19 (26.0)
Chronic renal disease, <i>n</i> (%)	6 (8.2)
Antiarrhythmic drugs after the 1st ExTRa-ABL	
Amiodarone, <i>n</i> (%)	14 (19.2)
Dose, mg	96 ± 13
Period of prescription, months (range)	17 ± 12 (2–33)
Pilsicainide, <i>n</i> (%)	1 (1.3)
Flecainide, <i>n</i> (%)	1 (1.3)

Note: All continuous values were expressed as the mean \pm SD.

Abbreviations: %M, ratio of the time recording multiple wavelets to the recording time; %M/%NP, ratio of multiple wavelets to nonpassive activations; %NP, ratio of the time recording nonpassive activation to the recording time; %R, ratio of the time recording meandering rotor to the recording time; AF, atrial fibrillation; BMI, body mass index; BNP, brain natriuretic peptide; ExTRa-ABL, ExTRa Mapping-guided rotor ablation; LA, left atrium; LVEF; left ventricular ejection fraction; NPA, nonpassively activated area; PVI, pulmonary vein isolation; TTE, transthoracic echocardiography.

endpoint, 45 of 73 (62%) patients were free from any atrial tachyarrhythmia at 12 months after the first ExTRa-ABL. Of the 28 patients with recurrence, five had recurrence of PAF or paroxysmal AT. In comparison between with and without recurrence, the non-PAF

TABLE 2 Patient and procedural characteristics.

	Without recurrence	With recurrence	p-Value
	n = 50 (68.5)	n = 23 (31.5)	
Male, n (%)	41 (82.0)	16 (69.6)	.23
Long-standing persistent AF, n (%)	22 (44.0)	19 (82.6)	.002
Age, year	63 ± 9	64 ± 8	.65
BMI	24.3 ± 3.5	24.9 ± 4.0	.56
Non-PAF duration, months	19 ± 22	56 ± 50	.002
Time since the diagnosis, months	64 ± 90	78 ± 68	.52
Follow-up period, months	37 ± 19	33 ± 14	.29
No. of prior PVIs	1.6 ± 0.8	1.6 ± 0.7	.94
BNP, pg/mL	177.9 ± 145.5	149.1 ± 113.0	.41
Complexity of rotor behavior			
%M/%NP	0.37 ± 0.14	0.39 ± 0.12	.20
TTE parameter			
LVEF, %	56 ± 9	56 ± 5	.86
LA diameter, mm	43 ± 6	46 ± 4	.02
Comorbid conditions			
CHA ₂ DS ₂ -VASc score	2.1 ± 1.4	2.0 ± 1.6	.97
CHADS ₂ score	1.3 ± 0.9	1.3 ± 1.3	.92
Hypertension, n (%)	35 (70.0)	14 (60.9)	.44
Diabetes mellitus, n (%)	12 (24.0)	4 (17.4)	.53
Stroke, n (%)	3 (6.0)	3 (13.0)	.37
Heart failure, n (%)	8 (16.0)	2 (8.7)	.49
Vascular disease, n (%)	4 (8.0)	0 (0.0)	.30
Mitral regurgitation, n (%)	14 (28.0)	5 (21.7)	.57
Chronic renal disease, n (%)	6 (12.0)	0 (0.0)	.17
Procedure time, min	195 ± 42	202 ± 54	.55
Direct termination of AF, n (%)	3 (6.0)	1 (4.3)	1.0
Amiodarone after the 1st session			
n (%)	10 (20.0)	4 (17.4)	0.53
Dose, mg	95 ± 16	100 ± 0	0.55
Period of prescription, months	14 ± 9	22 ± 14	0.26

Note: All continuous values were expressed as the mean ± SD.

Abbreviations: %M/%NP, ratio of multiple wavelets to nonpassive activations; AF, atrial fibrillation; BMI, body mass index; BNP, brain natriuretic peptide; LA, left atrium; LS-PersAF, long-standing persistent AF; LVEF, left ventricular ejection fraction; PVI, pulmonary vein isolation; TTE, transthoracic echocardiography.

duration prior to ExTRa-ABL was significantly longer (56 ± 50 vs. 19 ± 22 months, $p = .002$) and LA diameter was significantly larger (46 ± 4 vs. 43 ± 6 mm, $p = .02$). The details are given in Table 2.

The cumulative free rate from non-PAF/AT after 12 months was significantly higher in patients with non-PAF duration of ≤60 months prior to the first ExTRa-ABL (≤60M group) compared with >60 months (>60M group) (78.3% vs. 23.1%, $p < .001$, log-rank test; Figure 3A). The cumulative free rate from any atrial tachyarrhythmia after 12 months was also significantly higher in ≤60M group compared with >60M group (70.0% vs. 23.1%, $p = .001$, log-rank test; Figure 3B). There were no significant differences in primary and secondary outcomes between with and without direct AF termination. For the primary outcomes, non-PAF-free rate was 75.0% and 68.1% ($p = 1.0$), respectively. As well, freedom from any atrial tachyarrhythmia was 75.0% and 60.9% ($p = 1.0$), respectively. Non-PAF sustained even after achievement of modulation of NPAs could be terminated by internal cardioversion in all patients.

3.3 | A 3-year Kaplan–Meier analysis after ExTRa-ABL

With Kaplan–Meier analysis, cumulative arrhythmia-free rate from primary and secondary endpoint was 60.8% and 46.1%, respectively. For the primary outcome after ExTRa-ABL, significantly more patients in ≤60M group were free from non-PAF/AT compared with those in >60M group (68.9% vs. 23.1%, $p < .001$, log-rank test; Figure 4A). For the secondary outcome, significantly more patients in ≤60M group were free from any atrial tachyarrhythmia compared with those in >60M group (51.0% vs. 23.1%, $p < .01$, log-rank test; Figure 4B).

4 | DISCUSSION

The main findings of this study can be summarized as follows. First, freedom from non-PAF/AT recurrence at 12 months after

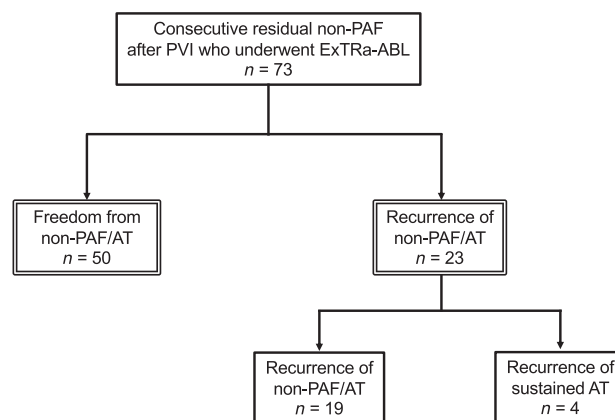


FIGURE 2 Patient flow chart. The first ExTRa-ABL was done in 73 non-PAF patients with non-PAF sustained after completion of PVI (residual non-PAF). Freedom from non-PAF/AT was observed in 50 of 73 patients. Of the 23 patients with recurrence, 19 had recurrence of non-PAF and four had that of sustained AT. AT, atrial tachycardia; ExTRa-ABL indicates the ExTRa Mapping-guided rotor ablation; non-PAF, nonparoxysmal atrial fibrillation; PAF, paroxysmal atrial fibrillation.

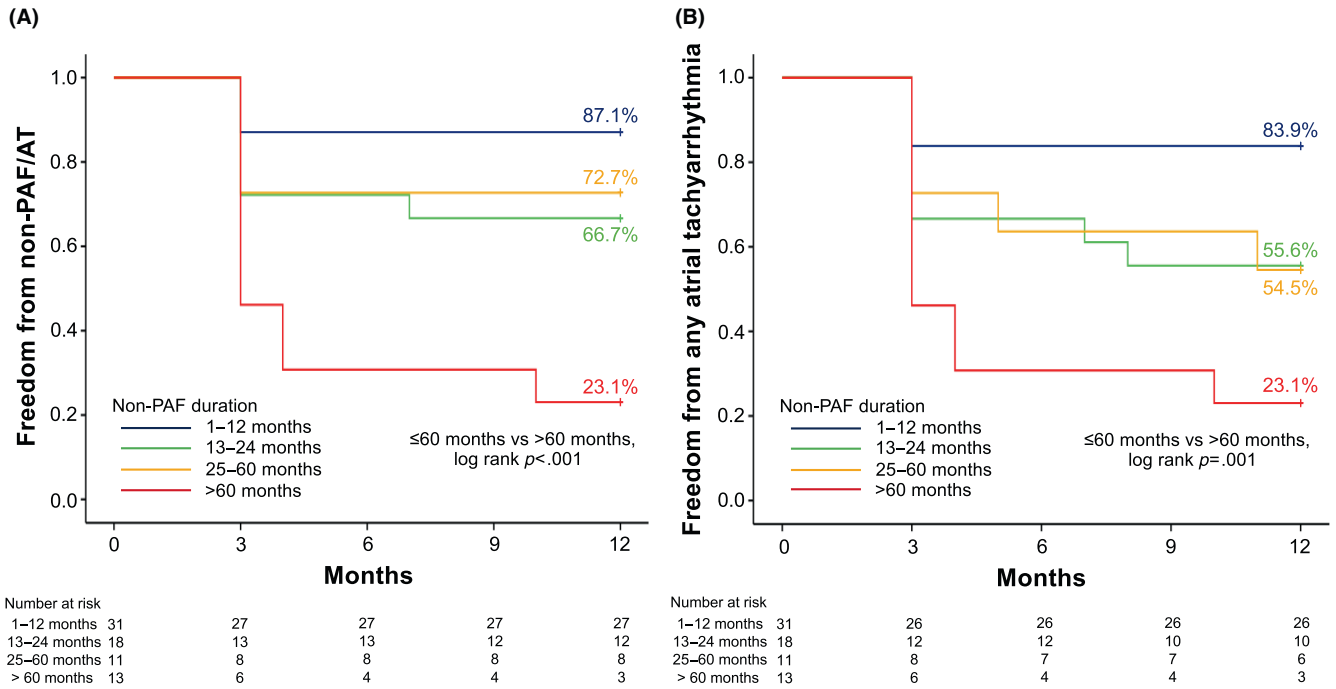


FIGURE 3 Kaplan-Meier analysis of freedom from non-PAF/AT and any atrial tachyarrhythmia at 12 months as a function of the non-PAF duration prior to the first ExTRa-ABL. (A) The cumulative rate of freedom from non-PAF/AT at 12 months after the first ExTRa-ABL. (B) The cumulative rate of freedom from any atrial tachyarrhythmia at 12 months after the first ExTRa-ABL. AT, sustained atrial tachycardia; ExTRa-ABL indicates the ExTRa Mapping-guided rotor ablation; non-PAF, nonparoxysmal atrial fibrillation.

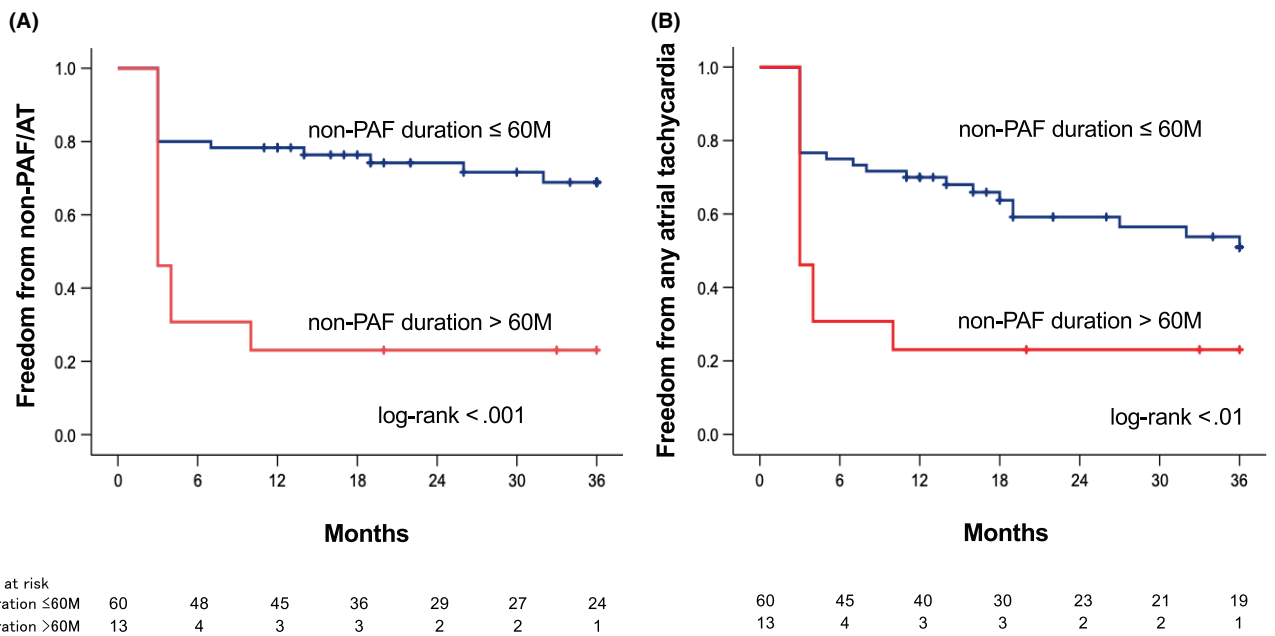


FIGURE 4 Kaplan-Meier estimates of the freedom from non-PAF and any atrial tachyarrhythmia in their relationship to the non-PAF duration. (A) The rate of freedom from non-PAF/AT after the first ExTRa-ABL in patients with a non-PAF duration of ≤60 months or >60 months. (B) The rate of freedom from any atrial tachyarrhythmia after the first ExTRa-ABL in the patients with a non-PAF duration of ≤60 months or >60 months. AT, sustained atrial tachycardia; ExTRa-ABL indicates the ExTRa Mapping-guided rotor ablation; non-PAF, nonparoxysmal atrial fibrillation.

ExTRa-ABL was achieved in 50 (69%) of patients. Second, non-PAF duration of ≤60 months prior to ExTRa-ABL was associated with a better outcome after ExTRa-ABL.

In the present study, the non-PAF duration prior to the first ExTRa-ABL was associated with a non-PAF/AT recurrence. This duration was significantly longer in non-PAF/AT recurrence group.

Scherr et al. reported that the non-PAF duration was an independent predictor of an atrial arrhythmia recurrence.¹¹ They also reported that the 5-year outcome of a stepwise ablation strategy had a 17% atrial arrhythmia-free rate after single ablation procedures in patients with 13 months of non-PAF duration.¹¹ Several groups have reported the importance of the non-PAF duration as a predictor of atrial arrhythmia recurrence after a stepwise ablation strategy, which was at most 2 years.^{12,13} In this study, to investigate the relationship between non-PAF duration and outcomes, the cut-out level of 60 months was selected retrospectively using the data in Figure 3. As far as we know, there was no report which showed the results of additional ablation strategies for patients with more than 2 years of non-PAF duration. In this study, our approach was found to be effective in approximately 70% of the ≤ 60 M group even after a single ablation procedure (Figures 3A and 4A), and showed to some extent in patients with non-PAF duration more than 2 up to 5 years. On the contrary, the effect of ExTRa-ABL was considered to be limited in patients with non-PAF duration > 60 months. Before this study, we expected that longer non-PAF duration would increase the complexity of excitation wave dynamics of rotors, and make them more likely to recur. However, the %M/%NP, the complexity of rotor behavior, had relationship with neither non-PAF duration nor non-PAF recurrence. Although there is a common belief that the complexity of rotor behavior led by atrial structural remodeling is involved in the mechanisms of AF persistence, the findings of this study indicate that the complexity of rotor behavior itself is not a direct determinant of the non-PAF ablation outcome.

Although some previous studies had reported the relationships between direct AF termination during additional ablation and outcomes, their results had been heterogeneous.^{7,11,14,15} In this study, only four patients had direct AF termination during ExTRa-ABL and direct AF termination had no correlation with better outcomes. But the number of patients with direct AF termination was small to discuss whether direct AF termination with additional ablation had an impact on outcome, in this study.

4.1 | Implications

The rotor ablation strategy for non-PAF, combining rotor detection and modulation under employing the ExTRa Mapping system, might be beneficial if the non-PAF duration prior to the first ExTRa-ABL was up to 60 months. This duration was longer than previously shown,^{11–14} and it might be helpful to know in advance what type of non-PAF would benefit from catheter ablation.

4.2 | Limitations

This study had several limitations. First, this study was a retrospective, single-arm observational study, and conducted at a single center, its results cannot be generalized. Additionally, the cut-out

level of 60 months was not prespecified value, but selected retrospectively. Second, the ablation operators were not blinded to the non-PAF duration. Information of the non-PAF duration could have caused a bias for the ablation procedures. Third, when proposing the ExTRa-ABL, whether the patient exhibited resistance to a PVI was determined by the attending physician, and there could have been a bias in the selection. In addition, even in patients with PVI reconnection confirmed at redo session, internal cardioversion was not performed just before the ExTRa-ABL to avoid missing the clinical mechanism of non-PAF persistence because of changes in AF wave dynamics. In these cases, it might remain possibility of sinus rhythm maintenance by cardioversion following PVI. Fourth, the quality of PVI might have been improving in the years of study period. Furthermore, contact force sensing catheter was not used in cases with ExTRa-ABL in index ablation. Therefore, it was very difficult to rule out the impacts of differences in the quality of PVI among cases. Finally, we did not performed follow-up with the long-time Holter recording in this study. It was possible that asymptomatic arrhythmia recurrence was missed.

5 | CONCLUSIONS

A non-PAF duration of 60 months or less prior to the first ExTRa-ABL was associated with a better ablation outcome. On the contrary, the effect of ExTRa-ABL was considered to be limited in patients with more than 60 months of non-PAF duration.

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CONFLICT OF INTEREST STATEMENT

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ETHICAL STATEMENT

This study was approved by the ethics committee of Shiga University of Medical Science. Reference number: R2015-046.

PATIENT CONSENT STATEMENT

Written informed consent for the ablation and participation in this study was obtained from all patients.

ORCID

Yusuke Okuyama  <https://orcid.org/0000-0001-7674-5728>

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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