Journal of Interventional Cardiac Electrophysiology (2019) 54:25–34
https://doi.org/10.1007/s10840-018-0436-x

MULTIMEDIA REPORT

Utility of acute arrhythmia termination as an ablation endpoint for induced atrial tachyarrhythmia after complete pulmonary vein isolation during catheter ablation for persistent atrial fibrillation

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Received: 1 April 2018 / Accepted: 3 August 2018 / Published online: 10 August 2018

Abstract

Purpose The presence of inducible atrial tachyarrhythmia after pulmonary vein isolation (PVI) during radiofrequency catheter ablation (RFCA) for persistent atrial fibrillation (AF) may indicate the necessity of further substrate modification, but the optimal ablation endpoint is unknown. We sought to assess the impact of procedural termination of inducible atrial tachyarrhythmia after PVI in comparison with continued atrial tachyarrhythmia after PVI.

Methods Among patients who underwent RFCA for persistent AF, we enrolled 93 patients who were in sinus rhythm after PVI and had inducible atrial tachyarrhythmia and 157 patients with continued atrial tachyarrhythmia after PVI. The impact of acute arrhythmia termination during further substrate modification on recurrence was compared between the two groups.

Results Acute termination was achieved in 51 (54.8%) patients in the induced arrhythmia group and 61 (38.9%) in the continued arrhythmia group. During a mean 35.8 months, acute termination did not significantly reduce arrhythmia recurrence in the induced arrhythmia group (HR 0.712, 95% CI 0.400–1.266, $p = 0.247$), while it was associated with improved outcome in the continued arrhythmia group (HR 0.590, 95% CI 0.355–0.979, $p = 0.038$). Acute termination of either induced atrial tachycardia (AT) or induced AF was not associated with improved procedure outcome. Among the continued arrhythmia group, the benefit of acute termination was statistically significant in AT (HR 0.329, 95% CI 0.108–0.997, $p = 0.039$), but not in AF (HR 0.704, 95% CI 0.396–1.253, $p = 0.233$) after PVI.

Conclusions Acute termination of induced rhythm is not a reliable ablation endpoint during substrate modification in patients with inducible arrhythmia after PVI.

Keywords Atrial fibrillation · Radiofrequency catheter ablation · Inducibility · Substrate modification

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10840-018-0436-x) contains supplementary material, which is available to authorized users.

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1 Introduction

Since the major role of the pulmonary vein (PV) in triggering atrial fibrillation (AF) was demonstrated, pulmonary vein isolation (PVI) has become the mainstay of non-pharmacological rhythm control strategies for AF [1–3]. However, the efficacy of PVI is limited in patients with persistent AF [4, 5], and PVI-only strategies for radiofrequency catheter ablation (RFCA) of persistent AF resulted in only 20% 1-year arrhythmia freedom in a systemic meta-analysis [6]. Various adjunctive ablation strategies including complex fractionated atrial electrogram (CFAE) ablation, linear ablation, venous structure other than PV ablation, and driver-guided ablation have been used to improve efficacy, but such substrate modification strategies do not have robust procedure endpoints.

Acute termination of AF during RFCA was associated with a higher probability of sinus rhythm (SR) maintenance and is a commonly used ablation endpoint for persistent AF [5, 7–9]. However, PVI while in SR allows better assessment of atrial tissue amplitude along the PV antrum and ensures effective PV isolation on the first attempt. Therefore, many physicians prefer to perform electrical cardioversion before or during RFCA for persistent AF [10]. AF non-inducibility after PVI can be used as a procedure endpoint in these patients and remnant inducible atrial tachyarrhythmia may indicate worse long-term outcomes and the necessity of further atrial substrate ablation [11, 12]. However, optimal ablation strategy for patients with inducible arrhythmia has not been well studied, and whether further substrate modification that terminates induced arrhythmia confers better procedure outcomes is unknown.

We sought to evaluate the prognostic impact of acute termination of induced atrial tachyarrhythmia during extra PV substrate ablation in patients with persistent AF. Using long-term cohort registry data for patients with persistent AF, we compared the effects of arrhythmia termination on arrhythmia freedom between patients with induced atrial tachyarrhythmia and continued atrial tachyarrhythmia after PVI.

2 Methods

2.1 Study population

We performed a single-center, observational study using registry data for patients with persistent AF who underwent RFCA from April 2009 to December 2015 in Seoul St. Mary's Hospital. The registry data included baseline characteristics of patients and detailed intra-procedural variables that were recorded at the time of RFCA. Persistent AF was defined as AF lasting more than 7 days, and all patients had ECG-documented symptomatic AF despite more than 6 weeks of antiarrhythmic drug (AAD) therapy. Among 304 patients with persistent AF, 54 who were in SR after PVI with no further inducible, sustained atrial tachyarrhythmia were excluded. The final study group included a total of 250 patients, which consisted of 93 who were in SR after PVI and had inducible, sustained atrial tachyarrhythmia and 157 with continued atrial tachyarrhythmia after PVI (Fig. 1). The study was approved by the institutional review board (IRB) of our institution.

2.2 Ablation procedure

All patients received anticoagulation before RFCA for at least 3 weeks, and the absence of left atrial appendage thrombus was confirmed by transesophageal echocardiogram or cardiac computed tomography scan before RFCA. Whether AADs were used before RFCA was left to the discretion of each physician. DC cardioversion was performed the day before RFCA in patients without documented SR in order to exclude permanent AF. Either an Ensite NavX (Abbot, St. Paul, MN, USA) or CARTO (Biosense Webster, Diamond Bar, CA, USA) 3D mapping system was used for detailed electro-anatomical mapping during RFCA. The ablation procedure was performed under deep sedation. After achieving an appropriate level of sedation, a vascular sheath was inserted, and infusion of intravenous heparin was started. Infusion dose or interval was adjusted to maintain blood activated coagulation time within 300–400 s throughout the procedure. A circular mapping catheter and an ablation catheter were advanced into the left atrium via double trans-septal accesses. The ablation procedure was performed using radiofrequency energy with an open irrigated catheter (Coolflex, Abbote, or Thermocool; Biosense Webster) with a power up to 35 W, which was decreased to 25 W during ablation on the posterior left atrial wall.

Initially, circumferential en bloc ablation of the entire PV antrum including part of posterior left atrium was performed. PVs were ablated in pairs and PV carina ablation was added when it was needed to achieve complete PVI. PVI was confirmed when entrance block was demonstrated during AF or both entrance and exit blocks were demonstrated during SR. If AF persisted after successful PVI, additional substrate modification was performed: roof line, perimitral isthmus/anterior line, and cavotricuspid isthmus line ablation were conducted first. In patients with continuing AF thereafter, ablation of inferior line, CFAE, and common sites of origin for non-PV AF triggers including superior vena cava, crista terminalis, coronary sinus, and the ligament of Marshall were added with the goal of intra-procedural arrhythmia termination. In patients with organized atrial tachycardia (AT), entrainment mapping with or without activation mapping was performed to identify the mechanism of AT, and appropriate sites were ablated to terminate AT. If patients were in SR after PVI, the exit block of PV was assessed, and additional ablation was performed as required. After confirmation of complete PVI,

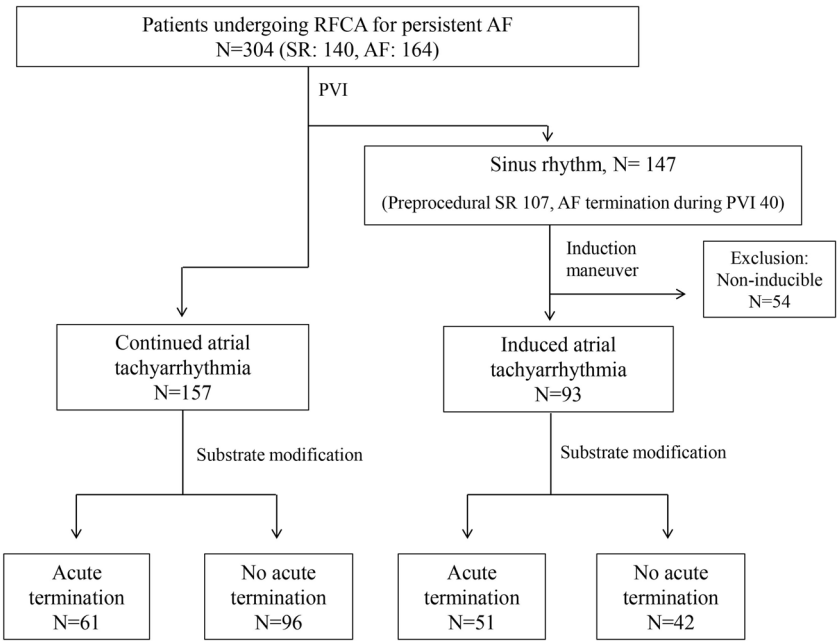


Fig. 1 Ablation approach and the patients classification. Among 304 patients undergoing RFCA for persistent AF, 54 patients without inducible arrhythmia after PVI were excluded. A total of 157 patients with continued atrial tachyarrhythmia after PVI and 93 patients with induced atrial tachyarrhythmia after PVI formed the final study group. During further substrate ablation, acute arrhythmia termination was achieved in 61 (38.9%) patients in the continued arrhythmia group and 51 (54.8%) in the induced arrhythmia group. SR, sinus rhythm; RFCA, radiofrequency catheter ablation; AF, atrial fibrillation; PVI, pulmonary vein isolation

an electrical induction maneuver using atrial burst pacing was performed, with a minimal pacing interval of 180 ms. Induced atrial tachyarrhythmia (AF/AT) was targeted for ablation only when it was sustained for more than 2 min. Patients who were unable to restore SR despite further ablation underwent electrical cardioversion. Before the end of the procedure, all patients were checked for the presence of bidirectional blocks after linear ablation and the absence of dormant PV conduction. If any incomplete blocks were identified, we conducted supplemental ablation.

2.3 Follow-up and outcome analysis

The primary endpoint was freedom from atrial tachyarrhythmia recurrence, defined as AF or AT lasting for more than 30 s that occurred after 3 months of blanking periods. Modes of recurrence were also analyzed and compared between patients with and without arrhythmia termination in the two groups. Patients were routinely scheduled to visit our outpatient clinic at 1 week; 1, 3, 6, and 12 months after RFCA; and every 6 months thereafter. We performed 12-lead ECG at every visit, and 24 h Holter tests were performed at 3, 6, and 12 months after RFCA and every 6 months thereafter. AADs were prescribed after RFCA at the duty physician's discretion.

2.4 Statistical analysis

For baseline characteristics, continuous variables are presented as mean ± standard deviation and compared using Student's t tests. Categorical variables are presented as frequencies with percentages (%) and compared by the χ^2 test or Fisher's exact test. Cumulative incidences of primary outcomes were estimated by Kaplan–Meier survival curves and compared with the results of log-rank tests. In the entire sample, we used multivariate Cox proportional hazard regression analysis to adjust for risk of the outcome of interest and to identify independent predictors. All significant variables in univariate Cox regression analysis and non-significant variables with proven prognostic importance were included in a multivariate Cox proportional hazards regression model. For all two-tailed comparisons, p values < 0.05 were considered to indicate statistical significance. All statistical analyses were performed using SPSS version 19 (SPSS Inc., Chicago, IL, USA).

3 Results

3.1 Baseline and procedure-related characteristics

Preprocedural electrical cardioversion was performed in 66/93 (71.0%) patients in the induced arrhythmia group and 56/157 (35.7%) in the continued arrhythmia group ($p < 0.001$). Among the induced arrhythmia group, SR was restored before extra PV ablation by preprocedural DC cardioversion in 62 (66.7%) patients, AF termination during PVI in 20 (21.5%) patients, and spontaneous AF termination before RFCA in 11 (11.8%) patients. Procedural arrhythmia termination during substrate modification was achieved in 51 (54.8%) patients in the induced arrhythmia group and in 61 (38.9%) patients in the continued arrhythmia group. Baseline characteristics according to the presence of acute arrhythmia termination in the two groups are shown in Table 1. In the induced arrhythmia group, there were no significant differences in all baseline

Table 1 Baseline characteristics in the two groups according to the presence of acute arrhythmia termination

	Induced arrhythmia ($N = 93$)			Continued arrhythmia ($N = 157$)		
	Acute termination $N = 51$	No acute termination $N = 42$	p value	Acute termination $N = 61$	No acute termination $N = 96$	p value
Age, years	60.4 ± 10.5	60.8 ± 9.9	0.844	61.6 ± 10.3	62.1 ± 10.8	0.778
Male, *n* (%)	41 (80.4%)	30 (71.4%)	0.311	45 (73.8%)	63 (65.6%)	0.283
Body mass index, kg/m^2	24.8 ± 3.2	25.5 ± 3.5	0.281	24.5 ± 3.4	24.9 ± 2.7	0.385
AF duration, months	30.0 ± 42.1	23.2 ± 31.4	0.388	34.8 ± 52.5	36.0 ± 49.5	0.889
AF duration > 12 months, *n* (%)	28 (56.0%)	16 (38.1%)	0.087	28 (45.9%)	49 (51.0%)	0.530
LA size, mm	44.6 ± 7.7	46.8 ± 4.7	0.109	44.1 ± 6.3	47.6 ± 7.4	0.004
LA volume, mL	152.6 ± 48.1	173.7 ± 61.1	0.178	167.4 ± 61.3	176.7 ± 59.1	0.436
Hypertension	25 (49.0%)	27 (64.3%)	0.140	39 (63.9%)	41 (42.7%)	0.010
Diabetes	6 (11.8%)	7 (16.7%)	0.497	11 (18.0%)	17 (17.7%)	0.959
Heart failure	4 (7.8%)	3 (7.1%)	0.899	1 (1.6%)	5 (5.2%)	0.256
Vascular disease	6 (11.8%)	4 (9.5%)	0.728	4 (6.6%)	7 (7.3%)	0.861
Stroke	4 (7.8%)	4 (9.5%)	0.798	11 (18.0%)	9 (9.4%)	0.113
CHA_2DS_2-Vasc score	1.7 ± 1.4	1.9 ± 1.3	0.453	2.0 ± 1.4	1.8 ± 1.6	0.377
CHA_2DS_2-Vasc score ≥ 2, *n* (%)	20 (39.2%)	23 (54.8%)	0.135	35 (57.4%)	47 (49.0%)	0.303
LVEF	58.7 ± 6.1	56.3 ± 8.8	0.142	59.4 ± 6.5	57.9 ± 8.3	0.239
Preprocedural DC cardioversion, *n* (%)	33 (64.7%)	33 (78.6%)	0.143	14 (23.0%)	42 (43.8%)	0.008
AAD discontinuation before procedure, *n* (%)	17 (34.0%)	9 (21.4%)	0.182	21 (34.4%)	26 (27.1%)	0.327
AAD use after 3 months, *n* (%)	38 (74.5%)	37 (88.1%)	0.090	38 (62.3%)	78 (81.3%)	0.008
Class Ic AADs	25 (49.0%)	15 (35.7%)	0.197	18 (29.5%)	32 (33.3%)	0.616
Amiodarone	8 (15.7%)	18 (42.9%)	0.004	12 (19.7%)	36 (37.5%)	0.018
Sotalol	4 (7.8%)	5 (11.9%)	0.510	5 (8.2%)	14 (14.6%)	0.232
Dronedarone	1 (2.0%)	0	0.362	3 (4.9%)	0	0.057

Categorical variables are presented as frequencies with percentages and continuous variables are presented as mean ± standard deviation. $P < 0.05$ is considered significant

AF atrial fibrillation, *LA* left atrium, *LVEF* left ventricular ejection fraction, *AAD* antiarrhythmic drug

characteristics between patients with and without acute arrhythmia termination. In the continued arrhythmia group, patients with acute termination showed significantly lower left atrial diameter (44.1 ± 6.3 vs. 47.6 ± 7.4 mm in the acute termination and no acute termination group, respectively, $p = 0.004$), higher prevalence of hypertension (63.9% vs. 42.7%, $p = 0.010$), and lower AAD prescription rate after RFCA (62.3% vs. 81.3%, $p = 0.008$). No significant difference was observed in terms of age, sex, body mass index, AF duration, or other underlying comorbidities between patients with and without acute arrhythmia termination. In both induced and continued arrhythmia group, post-RFCA prescription rate of amiodarone was higher in patients without acute termination. The baseline characteristics and AAD prescription rates were not different between the induced and continued arrhythmia groups, except for the frequency of preprocedural electrical cardioversion (Supplemental Table 1).

Procedure-related characteristics are shown in Table 2. There was a non-significant trend toward longer procedure time, fluoroscopy time, and ablation time for patients without acute termination in both induced and continued arrhythmia group. PVI was successful in 97.6% of all included patients. In the induced arrhythmia group, induced rhythm after PVI was AF in 38 (40.8%) and AT in 55 (59.2%) patients, and acute termination was mostly achieved in AT (80.4%). In the continued arrhythmia group, the rhythm after PVI was AF in 124 (79.0%) and AT in 33 (21.0%) patients, and the acute termination rates were similar (39.5% vs. 36.4% for continued AF and AT, respectively, $p = 0.741$). In both induced and continued arrhythmia groups, frequency of CFAE ablation was not significantly different between patients with and without acute termination. More than one linear ablation was performed in 240 (96.0%) patients. Roof line ablation, inferior line ablation, and anterior line ablation were more frequently performed in patients without acute termination in both groups. The overall success rates of roof line, inferior line, perimitral isthmus line, anterior line, and cavotricuspid isthmus line were 94.6%, 95.2%, 84.5%, 78.7%, and 99.5%. There was no significant difference in the success rate of linear

Table 2 Procedure-related characteristics in the two groups according to the presence of acute arrhythmia termination

	Induced arrhythmia ($N = 93$)			Continued arrhythmia ($N = 157$)		
	Acute termination $N = 51$	No acute termination $N = 42$	p value	Acute termination $N = 61$	No acute termination $N = 96$	p value
Procedure time, min	214.6 ± 50.1	222.5 ± 48.7	0.229	215.7 ± 52.7	227.4 ± 76.7	0.365
Fluoroscopy time, min	67.8 ± 25.4	79.6 ± 41.7	0.216	72.5 ± 37.1	80.9 ± 37.6	0.252
Ablation time, min	75.2 ± 30.4	85.6 ± 39.6	0.322	73.5 ± 28.1	83.7 ± 29.6	0.087
Targeted rhythm after PVI						
Atrial fibrillation	10 (19.6%)	28 (66.7%)	< 0.001	49 (80.3%)	75 (78.1%)	0.741
Organized atrial tachycardia	41 (80.4%)	14 (33.3%)		12 (19.7%)	21 (21.9%)	
CFAE ablation, *n* (%)	17 (33.3%)	12 (28.6%)	0.622	26 (42.6%)	42 (43.8%)	0.890
Linear ablation, *n* (%)						
Roof line	37 (72.5%)	40 (95.2%)	0.004	43 (70.5%)	85 (88.5%)	0.005
Inferior line	22 (43.1%)	30 (71.4%)	0.006	22 (36.1%)	71 (74.0%)	< 0.001
Perimitral isthmus	18 (35.3%)	17 (40.5%)	0.608	36 (59.0%)	45 (46.9%)	0.138
Anterior line	12 (23.5%)	21 (50.0%)	0.008	15 (24.6%)	46 (47.9%)	0.003
Cavotricuspid isthmus	43 (84.3%)	35 (83.3%)	0.898	56 (91.8%)	81 (84.4%)	0.174
SVC isolation	2 (3.9%)	9 (21.4%)	0.009	15 (24.6%)	30 (31.3%)	0.368

Categorical variables are presented as frequencies with percentages and continuous variables are presented as mean ± standard deviation. $P < 0.05$ is considered significant

PVI pulmonary vein isolation, *CFAE* complex fractionated atrial electrograms, *SVC* superior vena cava

block between patients with and without acute termination in either induced or continued arrhythmia group.

3.2 Procedure outcomes

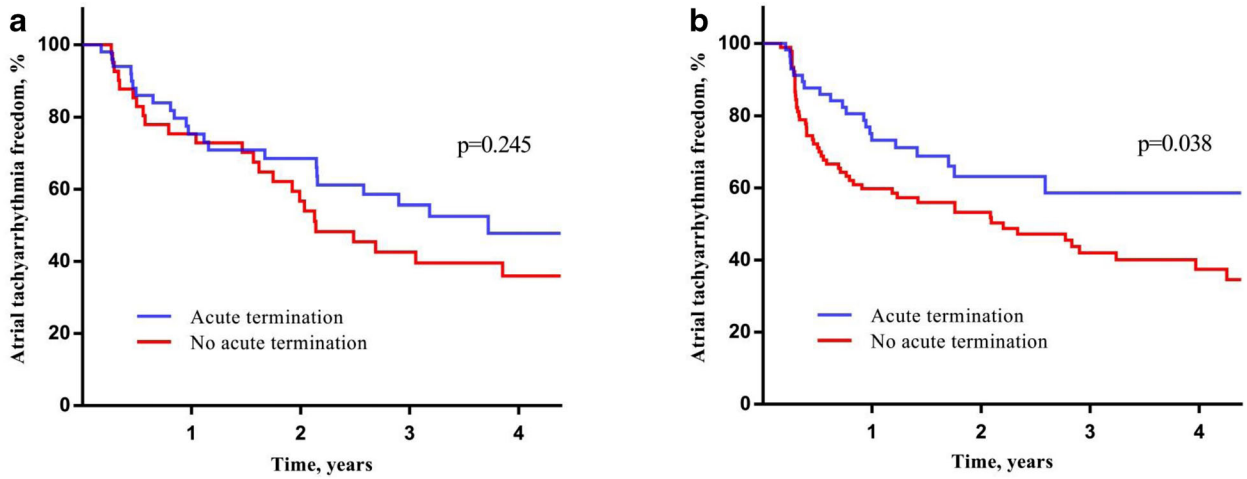
The mean follow-up duration was 35.8 (± 21.0) months. In the induced arrhythmia group, the atrial tachyarrhythmia freedom on-/off-AAD was higher in patients with acute termination, but this putatively beneficial effect was not statistically significant [56.9% vs. 38.1% in patients with and without acute termination, hazard ratio (HR) 0.712, confidence interval (CI) 0.400–1.266, $p = 0.247$] (Fig. 2a). Also, the improvement in arrhythmia freedom off-AAD was not significant (19.6 and 7.1%, HR 0.283, 95% CI 0.076–1.051, $p = 0.059$). On the other hand, in the continued arrhythmia group, acute arrhythmia termination was associated with significantly higher atrial tachyarrhythmia freedom on-/off-AAD (65.6% vs. 44.8%, HR 0.590, 95% CI 0.355–0.979, $p = 0.038$) and off-AAD (31.1% vs. 13.5%, HR 0.444, 95% CI 0.217–0.909, $p = 0.027$) (Fig. 2b). According to the mode of recurrence, acute arrhythmia termination did not affect the recurrence of either AT or AF in the induced arrhythmia group. In the continued arrhythmia group, acute termination was associated with a significant reduction in recurrent AF (20.0% vs. 35.4%, $p = 0.048$) (Fig. 3). Between the induced arrhythmia group and continued arrhythmia group, there was no significant difference in overall atrial tachyarrhythmia freedom (51.6% vs. 47.1% in the induced arrhythmia and the continued arrhythmia group, $p = 0.398$) (Supplemental Fig. 1).

According to the induced rhythm, neither induced AF nor AT significantly benefited from acute termination (Fig. 4a, b). In the continued arrhythmia group, acute termination significantly reduced arrhythmia recurrence in patients with AT after PVI (HR 0.329, 95% CI 0.108–0.997, $p = 0.039$) but not in patients with AF after PVI (HR 0.704, 95% CI 0.396–1.253, $p = 0.233$) (Fig. 4c, d). Remarkably, patients who achieved continued AT termination had the most favorable outcomes (22.2% recurrence rate), and patients in whom continued AT was not terminated by ablation had the worst outcomes (71.4% recurrence rate).

In univariate analysis conducted using the entire sample, low left atrial diameter and the presence of acute arrhythmia termination were associated with improved arrhythmia freedom (Table 3). In multivariate analysis, the presence of acute arrhythmia termination was not an independent predictor for improved outcome (HR 0.704, 95% CI 0.476–1.042, $p = 0.079$) after adjusting for left atrial diameter, AF duration ≥ 1 year, and arrhythmia continuation after PVI. Only left atrial diameter was independently associated with higher arrhythmia recurrence in the overall population (HR 1.033, 95% CI 1.007–1.059, $p = 0.012$).

3.3 Complications

Overall, the major complication rate was 5.6%, and cardiac tamponade was the most common complication (4.0%)



Number at risk

Acute termination	51	34	29	19	9
No acute termination	42	30	21	14	8

Number at risk

Acute termination	61	41	20	11	7
No acute termination	96	52	37	24	14

Fig. 2 Comparison of long-term arrhythmia freedom on-/off-antiarrhythmic drugs between patients with and without acute arrhythmia termination in the induced arrhythmia group (**a**) and the continued arrhythmia group (**b**)

(Table 4). No cases of esophageal rupture or atrioesophageal fistula developed, and there were no complications that led to death or major sequelae. In the induced arrhythmia group, cardiac tamponade was developed in three patients (5.9%) with acute termination, and no major complications occurred in patients without acute termination ($p = 0.249$). In the continued arrhythmia group, the procedural complication rates were similar between patients with and without acute termination (6.6% vs. 7.3%, $p = 0.861$).

4 Discussion

In this study, achieving acute arrhythmia termination during substrate modification resulted in only non-significant benefits to patients with inducible arrhythmia after PVI, but was associated with significant improvements in procedure outcomes among patients with continued arrhythmia after PVI. Among the continued arrhythmia group, the benefit of acute arrhythmia termination was more pronounced in patients with

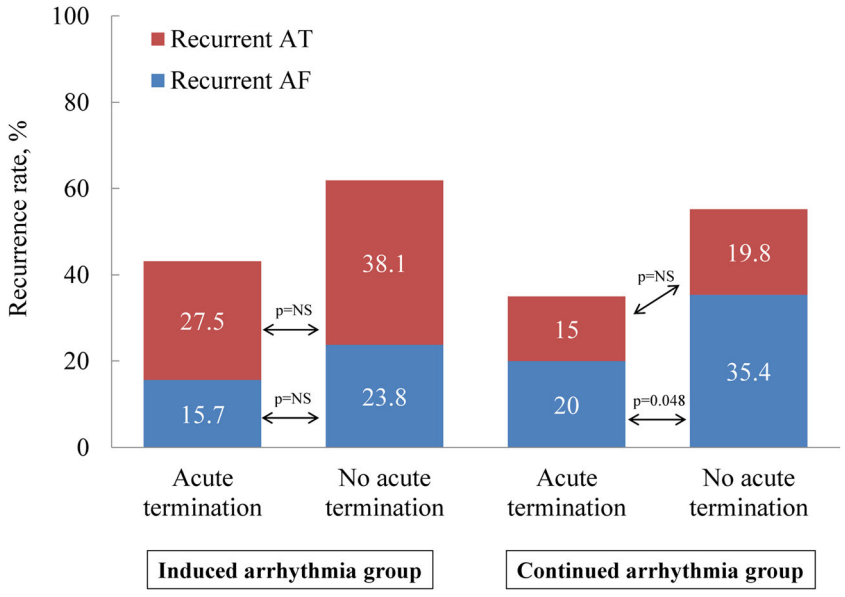


Fig. 3 Mode of recurrence according to the presence of acute arrhythmia termination in the two groups. Only the incidence of recurrent AF in the continued arrhythmia group was significantly reduced for patients with acute termination. AT, atrial tachycardia; AF, atrial fibrillation; NS, non-specific

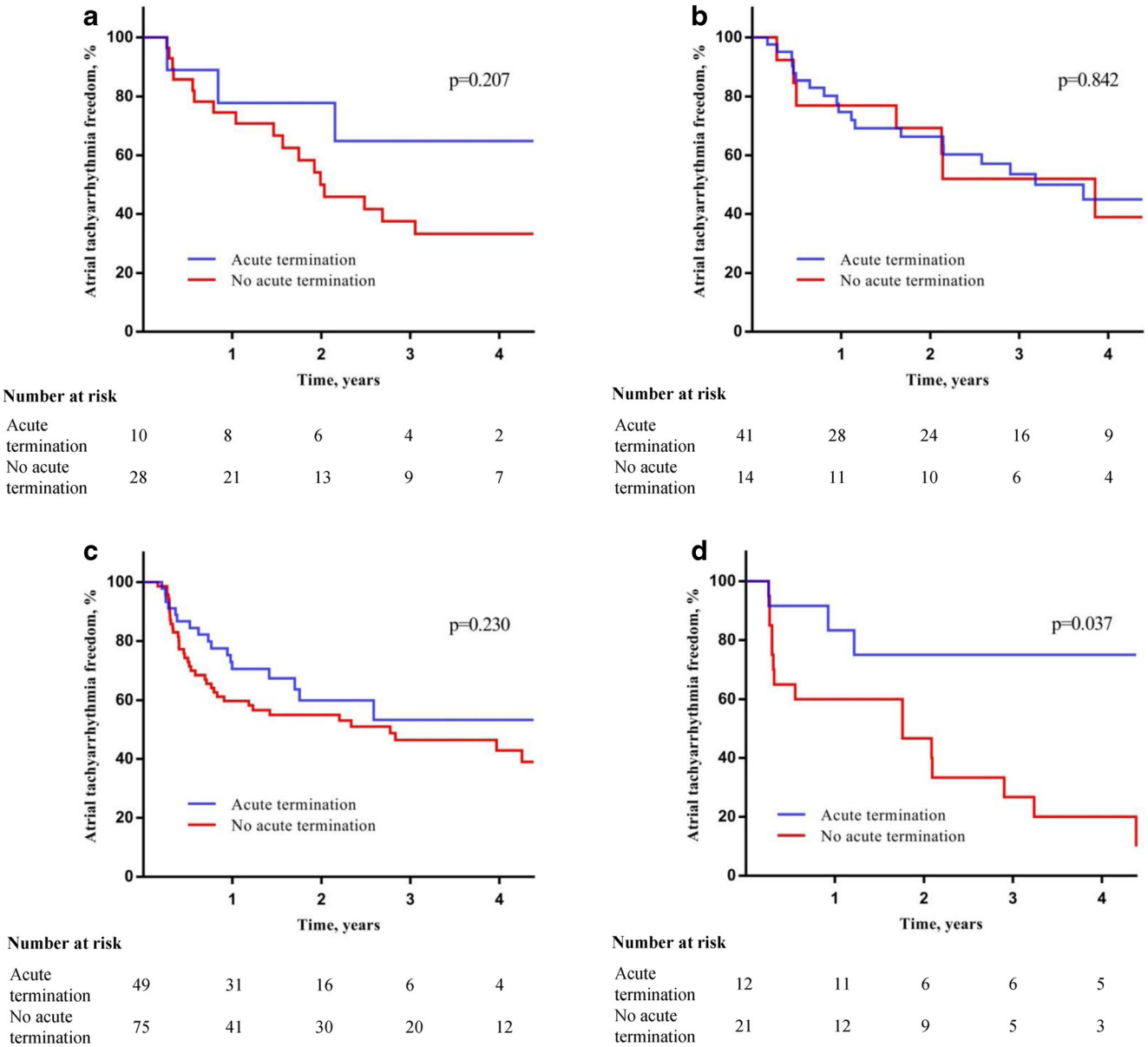


Fig. 4 Comparison of long-term arrhythmia freedom between patients with and without acute arrhythmia termination according to the rhythm after PVI targeted for further ablation. In the induced arrhythmia group, acute arrhythmia termination was not significantly associated with improved arrhythmia freedom in patients with either AF (**a**) or AT (**b**) after PVI. In the continued arrhythmia group, the benefit of acute arrhythmia termination was not significant in patients with AF (**c**), but was clearly shown in patients with AT (**d**) after PVI. AF, atrial fibrillation; AT, atrial tachycardia; PVI, pulmonary vein isolation

organized AT after PVI than in those with AF after PVI. However, achieving acute termination was not clearly beneficial in either induced AT or AF patients in the induced arrhythmia group. Procedural termination of AF is commonly used as a procedure endpoint for persistent AF ablation, but our findings showed the limited value of this endpoint in induced atrial tachyarrhythmia.

Whether additional substrate ablation would confer incremental benefits over complete PVI in patients with persistent AF remains controversial [13, 14]. Recent STAR AF II trial [13] showed no beneficial effect of either linear ablation or CFAE ablation in addition to PVI. Although the results from randomized studies do not support routine addition of any certain type of substrate modification after PVI, a number of studies have reported the benefits of stepwise approach beyond PVI targeting the termination of persistent AF [7–9] or the necessity of further ablation in patients with inducible AF after PVI [11, 12, 15]. In patients with SR after completion of planned ablation, the frequency of AF induction by burst pacing maneuver was 10–30%, and the organized AT induction rate was similar or even higher (10–56%) [16–19]. Several previous studies have demonstrated the benefit of further

Table 3 Predictors of atrial tachyarrhythmia recurrence in the overall population

	Univariate analysis			Multivariate analysis*		
	Hazard ratio	95% confidence interval	*p* value	Hazard ratio	95% confidence interval	*p* value
Age, years	1.005	0.989–1.022	0.545			
Male	0.882	0.599–1.300	0.526			
Structural heart disease	1.263	0.554–2.876	0.579			
CHA_2DS_2-Vasc score ≥ 2	1.077	0.753–1.541	0.684			
Left atrial diameter	1.037	1.012–1.063	0.003	1.033	1.007–1.059	0.012
AF duration ≥ 1 year	1.173	0.820–1.679	0.383	1.246	0.867–1.790	0.234
Preprocedural DC cardioversion	1.046	0.731–1.497	0.807			
Arrhythmia continuation after PVI	1.171	0.811–1.689	0.399	1.116	0.767–1.625	0.567
Organized AT after PVI	0.956	0.661–1.383	0.810			
Acute arrhythmia termination	0.641	0.442–0.931	0.019	0.704	0.476–1.042	0.079

*In multivariate analysis, hazard ratio was adjusted for left atrial diameter, AF duration ≥ 1 year, and arrhythmia continuation after PVI

AF atrial fibrillation, *PVI* pulmonary vein isolation

ablation in inducible patients. Oral et al. randomly divided patients with paroxysmal AF in whom AF was still present or induced after complete PVI into a no further ablation group and an additional substrate modification group [15]. In that study, further ablation in arrhythmia-inducible patients was associated with significant improvements in arrhythmia freedom. More recently, Nagamoto et al. also found that successful ablation of inducible ATs after AF termination resulted in lower AT recurrence [19]. Although further ablation after PVI may confer additional benefits in inducible patients, our study showed that procedural termination of induced atrial tachyarrhythmias was not a reliable ablation endpoint. There are several possible explanations for this observation: first, induced rhythm is not always correlated to clinically relevant arrhythmia. In a subgroup study by Oral et al., 67% of patients with continued or inducible AF after PVI remained recurrence-free during follow up. Another study showed that induced ATs during ablation did not necessarily become clinical ATs [19]. Moreover, whether aggressive stimulation protocols would lead to further benefit is also doubtful [17, 18]. Because the clinical significance of inducible AF/AT is not clear, the possibility is lower that additional ablation targeting inducible rhythms would successfully modify the critical atrial substrate that is relevant for clinical recurrence. Second, while patients with persistent AF have sustained arrhythmia for more than a week, induced rhythms are commonly targeted for ablation when they persist for more than 1–2 min. Thus, induced rhythms are more likely to be self-terminating, and spontaneous termination can occur during RFCA. This may be misinterpreted as achievement of successful substrate ablation. The use of stricter selection criteria to identify AF inducibility or modification of stimulation maneuvers may increase the efficacy of further ablation strategies. This question requires further investigation.

Patients with continued arrhythmia after PVI in our study showed improved arrhythmia freedom with acute termination, and the impact was pronounced in AT but was not significant in AF. ATs spontaneously organized from AF are likely to be associated with recurrent AT of the same type [9, 20, 21]. It is noteworthy that patients with continued ATs after PVI that was not terminated at the end of RFCA had the worst long-term prognosis, and patients with continued AT termination

Table 4 Complication rates according to the presence of acute arrhythmia termination in the two groups

	Induced arrhythmia (*N* = 93)		Continued arrhythmia (*N* = 157)	
	Acute termination *N* = 51	No acute termination *N* = 42	Acute termination *N* = 61	No acute termination *N* = 96
Procedural complication, *n* (%)	3 (5.9%)	0	4 (6.6%)	7 (7.3%)
Cardiac tamponade	3 (5.9%)	0	4 (6.6%)	3 (3.1%)
Stroke	0	0	0	1 (1.0%)
Major groin hematoma	0	0	0	2 (2.1%)
Retroperitoneal hemorrhage	0	0	0	1 (1.0%)

All variables are presented as frequencies with percentages

had the most favorable prognosis. These results imply that intermediate AT spontaneously organized from AF during PVI is a clinically important source of recurrence and should be more intensively treated in comparison to inducible ATs.

Although procedural termination of arrhythmia in patients with non-paroxysmal AF has been shown to be an independent predictor of procedural success [5, 8, 9, 22], whether better prognosis after achieving acute arrhythmia termination occurs due to adequate ablation or lower baseline arrhythmogenicity of the left atrium cannot be clearly differentiated. In the previous studies, left atrial diameter was smaller in patients with procedural AF termination [8, 9]. Similarly, in our study, baseline left atrial diameter was significantly smaller in patients with acute termination in the continued arrhythmia group, while this difference was not observed in the induced arrhythmia group. It is plausible that lower baseline left atrial arrhythmogenicity significantly contributed to intraprocedural AF termination and mediated improvements in arrhythmia freedom. However, although patients achieving SR by ablation have lower arrhythmogenicity, acute arrhythmia termination can still serve as a reliable procedure endpoint because substrate modification is likely to be more successful in patients having less abnormal substrates.

4.1 Clinical implications

During RFCA for persistent AF, induction tests after planned ablation may yield inducible arrhythmia, which might in turn lead to consideration of further ablation. There are no established procedural endpoints during ablation for induced arrhythmia, and our study demonstrates that the termination of induced arrhythmia is not a reliable endpoint, unlike those for continued arrhythmia. Patients with SR after PVI would not benefit from extensive ablation in the pursuit of induced arrhythmia termination because inducible arrhythmias do not necessarily result in clinical recurrence. The identification of effective ablation strategies in inducible patients should be a goal of future studies.

4.2 Limitations

Our study is a retrospective study without a fixed protocol for RFCA, and differences in the baseline variables and ablation strategies among groups were unavoidable. Also, there is a potential of under-recognition of asymptomatic recurrence, which cannot be fully detected by periodic ECG or Holter monitoring. However, there were no statistically significant differences in baseline characteristics between patients with and without acute termination among the induced arrhythmia group. In the induced arrhythmia group, patients with no acute termination showed higher frequency of inferior line or anterior line ablation, but this was also observed in the continued arrhythmia group; therefore, it is not likely that choice of ablation strategy significantly affected the impacts of acute termination. Second, the induced arrhythmia group had high heterogeneity because patients who have undergone electrical cardioversion before RFCA, patients with spontaneous SR, and patients with restored SR during PVI were all included in the induced arrhythmia group. Nevertheless, arrhythmia induction tests are commonly used in all of the above circumstances, indicating that our study has many important implications. Third, the time duration of our study enrollment was relatively long (6 years). Although we used consistent ablation strategies for persistent AF during the study period, the details on ablation protocol may have differed among the subjects. Finally, the procedural arrhythmia termination rate in our study is lower than previous studies, even considering that the patients in whom AF was terminated during PVI were excluded in our study [7–9].

5 Conclusion

During catheter ablation for persistent AF, patients with inducible atrial tachyarrhythmia after PVI did not significantly benefit from acute arrhythmia termination by further extra PV ablation, in contrast to patients with continued atrial tachyarrhythmia after PVI. Inducible atrial tachyarrhythmia after PVI may indicate the presence of remnant abnormal atrial substrate; however, procedural termination of induced arrhythmia is not an adequate endpoint for substrate modification.

Acknowledgements We would like to thank Seo Seung-Duk, Abbott Cardiac Rhythm Management Division, for his efforts in literature review and correction of the paper.

Compliance with ethical standards

Conflict of interest None declared.

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