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Early choice for catheter ablation reduced readmission in management of atrial fibrillation: Impact of diagnosis-to-ablation time

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ABSTRACT

Background: The impact of delays in the treatment with radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF) has not been well evaluated. The aim of this study was to investigate the impact of diagnosis-to-ablation time (DAT) on the long-term clinical outcomes after AF-RFCA.
Methods: We enrolled 1206 consecutive patients undergoing first-time RFCA for AF. The study population was divided into 2 groups based on DAT: short (<3 years) (N = 675) and long (>3 years) (N = 531) DAT groups.
Results: Mean follow-up duration was 5.0 ± 2.5 years. The 5-year event-free rates from recurrent atrial tachyarrhythmias after the first and second RFCAs were significantly higher in short DAT group than in long DAT group (60.2% versus 48.3%, log-rank $P < 0.001$; 83.2% versus 75.2%, log-rank $P = 0.02$, respectively), leading to reduced cardiovascular hospitalization in short DAT group. After adjusting baseline differences, short DAT was independently associated with lower arrhythmia recurrence rates after the first and second RFCAs (hazard ratio [HR] 0.72, 95% confidence interval [CI] 0.60–0.86 and HR 0.72, 95%CI 0.55–0.95, respectively). There were no significant differences between the 2 groups in the event-free rates from all-cause and cardiovascular deaths, heart failure hospitalization, and ischemic stroke. However, among patients with a history of heart failure or reduced left ventricular function, the event-free rate from heart failure readmission was significantly higher in short DAT group (85.0% versus 61.0%, $P = 0.004$).
Conclusions: In the management of AF, early RFCA was associated with significantly lower arrhythmia recurrence compared with delayed RFCA, leading to reduced cardiovascular hospitalization, especially in heart failure patients.

1. Introduction

Atrial fibrillation (AF) is a progressive disease associated with increased risk of morbidities and mortality [1–2]. AF itself promotes electrophysiological and structural remodeling of atrium, known as "AF begets AF" [3]. Paroxysmal AF gradually develops to persistent AF with annual rates of 5.5–8.6% [4–5]. Because of this progressive nature, suppression of AF is important to slow down the atrial remodeling and thereby maintain sinus rhythm. However, usage of antiarrhythmic drugs (AADs) is associated with low success rate in suppressing AF and substantial risk for adverse events, especially in high-risk patients [6–7].

Radiofrequency catheter ablation (RFCA) for AF is an invasive rhythm control therapy, which was shown to be superior to AADs in suppressing AF in several randomized controlled trials [8–11]. In the recent guidelines, RFCA as a second-line therapy for drug-refractory paroxysmal AF has been recommended as class I indication, and RFCA as a first-line therapy for paroxysmal AF without prior AAD use has been recommended as class IIa indication [12,13]. Although delayed diagnosis-to-ablation times (DATs) were reported to be associated with lower success rates of RFCA for AF [14–16] the impact of the treatment delay on the long-term clinical outcomes of AF ablation has been rarely evaluated. Therefore, we sought to investigate the impact of DAT on the long-term arrhythmia-free survival and clinical outcomes after AF ablation from a large scale registry enrolling over 1200 consecutive patients with high follow-up rate [17].

2. Methods

2.1. Study population

We retrospectively enrolled 1206 consecutive patients undergoing first-time RFCA for AF in Kyoto University Hospital between February 2004 and March 2015. Written informed consent was obtained from all patients. Patients were divided into 2 groups based on DAT: short (<3 years) DAT (N = 675) and long (> 3 years) DAT (N = 531)

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groups. DAT was defined as the time interval from the first diagnosis of AF to the first RFCA for AF. Follow-up information was obtained by review of hospital-chart and/or contact with the patient, relatives, and/or referring physicians. Final follow-up rate reached 99.3%. The study protocol was approved by the institutional review board of Kyoto University Hospital. We have previously reported the detailed protocol of the study as well as the acute and long-term general clinical outcomes of the RFCA procedure for AF in this study population [17].

2.2. Ablation procedure protocol and post-procedural management

Extensive encircling pulmonary veins (PVs) isolation was performed with two 20-polar circular-shaped catheters placed in ipsilateral superior and inferior pulmonary veins. Superior vena cava was isolated whenever necessary. Tricuspid valve isthmus ablation was routinely performed regardless of the presence of typical atrial flutter. Additional complex fractionated atrial electrogram (CFAE) ablation was performed when sinus restoration was not obtained after PVI or AF was easily induced by electrical stimulation from the atrium and/or isoproterenol infusion. Additional left atrial (LA) linear ablations such as mitral isthmus line and LA roof line ablations were performed for sustained atrial tachycardias during the procedure. The ablation catheter used for PV isolation and LA linear ablations was an 8-mm tip catheter (Fantasista, Japan Lifeline, Tokyo, Japan and NAVISTAR, Biosense Webster, CA, USA) from 2004 to 2009, and a 3.5-mm tip irrigation catheter (NAVISTAR THERMOCOOL, Biosense Webster, CA, USA) from 2010 to 2015 [17].

After the first procedure, oral anticoagulant (OAC) was continued for at least 3 months. Thereafter, discontinuation of OAC in patients without arrhythmia recurrence was left to the discretion of the attending physician. AADs were discontinued before the RFCA procedure, and were restarted only when recurrent atrial tachyarrhythmias were detected. The second procedure was recommended to the patients with recurrent atrial tachyarrhythmias after the blanking period of 3 months. The strategy of the second procedure was first to check the presence or absence of LA-PV reconnections. If LA-PV reconnections were detected, re-isolation of PVs was performed. The additional ablation strategy was the same as that in the first procedure.

2.3. Outcome measures and statistical analysis

The primary outcome measures were the event-free survival from recurrent atrial tachyarrhythmias with a blanking period of 90 days after the first and the second ablation procedures. For patients who received only 1 procedure, arrhythmia-free interval after the second procedure was accounted for the interval after the first procedure. The recurrent atrial tachyarrhythmias were defined as documented AF and/or atrial tachycardia (AT) lasting for >30 s or those requiring repeat ablation procedures. A 12 lead electrocardiogram was routinely measured at each clinical visit and 24-hour Holter monitoring was recommended at 3-, 6-, 12-month and yearly thereafter. The secondary outcome measures included the event-free rates from all-cause death, cardiovascular death, heart failure hospitalization, ischemic stroke, and cardiovascular hospitalization. Cardiovascular hospitalization included readmission for any cardiovascular cause such as second procedure, heart failure exacerbation, ischemic and hemorrhagic stroke, major bleeding, myocardial infarction, coronary or peripheral artery revascularization, device implantation, and all-cause death.

AF was classified into paroxysmal (lasting <7 days) and non-paroxysmal (lasting ≥7 days) AF. Congestive heart failure (CHF) as a component of $CHADS_2$ and CHA_2DS_2-VASC scores included hospitalization for exacerbation of heart failure within 100 days before the index RFCA procedure and/or left ventricular ejection fraction of <40%. Stroke was defined as neurological deficit requiring hospitalization with symptoms lasting for >24 h. Stroke as a component of $CHADS_2$ and CHA_2DS_2-VASC scores included ischemic stroke and transient ischemic attack (TIA).

Categorical variables were presented as number and percentage and were compared with the chi-square test or Fisher's exact test. Continuous variables were presented as mean and standard deviation or median with interquartile range, and were compared using the Student's *t*-test or Wilcoxon rank sum test based on their distributions. The event-free rate was estimated by the Kaplan-Meier method, and the differences were assessed by the log-rank test.

The Cox proportional hazard analyses were performed to evaluate univariate and multivariate influence of DAT on recurrent atrial tachyarrhythmias after the first and the second procedures with 10 clinically relevant variables (listed in Table 1). Continuous variables were dichotomized by clinically meaningful reference values. Statistical analyses were performed using JMP 10 (SAS Institute Inc., Cary, NC) software. All the analyses were two-tailed, and *P* value of <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

Mean age of the current study population was 64 years and 29% of patients were female (Table 1). Median DAT was 2.4 years and DAT became gradually shorter during the enrollment period over time (Supplementary Fig. 1).

Mean $CHADS_2$ and CHA_2DS_2-VASc scores were 1.2 and 2.0, respectively. Mean LA diameter was 39 mm. Regarding the procedure characteristics, PV isolation and tricuspid valve isthmus ablation were successfully completed in most patients. After successful PV isolation, 30% of patients received additional SVC isolation.

The median of DAT was 0.7 year in short DAT group and 6.9 years in long DAT group. Previous rhythm control by AADs had been less frequently performed in short DAT group (36.6% versus 42.4%, $P = 0.04$). The prevalence of CHF was significantly higher in short DAT group (9.9% versus 6.6%, $P = 0.04$). Conversely, short DAT group had significantly lower prevalence of previous ischemic stroke or TIA and lower $CHADS_2$ score compared with long DAT group. There were no significant differences between the groups in echocardiographic findings, including LA diameter. The prevalence of additional ablation procedure was comparable between the 2 groups.

During DATs, paroxysmal AF at the time of first AF documentation had developed to persistent AF in 214 (20.1%) out of 1067 patients (Supplementary Fig. 2-A). The transition was less prevalent in short DAT group than in long DAT group (16.4% versus 24.2%, $P = 0.002$). The cumulative incidence of AF perpetuation during DAT was 6.5% at 1-year, 14.9% at 3-year, 21.8% at 5-year, and 34.4% at 10-year (Supplementary Fig. 2-B).

3.2. Ischemic stroke or TIA before ablation

Among 119 patients with prior ischemic stroke or TIA, AF had been documented before the events in 51 patients (42.9%). However, only about half of those patients had been administered OAC at the time of the events (Supplementary Table 2). The prevalence of prior ischemic stroke or TIA after documentation of AF was significantly lower in short DAT group (20.4% versus 58.6%, $P < 0.001$).

3.3. Arrhythmia recurrence after AF ablation

Mean follow-up duration was 5.0 ± 2.5 years. The event-free rate from recurrent atrial tachyarrhythmias after the first RFCA procedure was significantly higher in short DAT group than in long DAT group (60.2% versus 48.3% at 5-year, long-rank $P < 0.001$) (Fig. 1). The cumulative incidence of the second RFCA procedure was significantly lower in short DAT group (29.9% versus 38.6% at 5-year, $P = 0.002$). Among the entire 403-second procedures, excluding 4 procedures performed at other institutions, the prevalence of PV re-isolation and additional ablation procedures were not significantly different between the 2 groups (Supplementary Table 1). The event-free rate from recurrent atrial tachyarrhythmias after the second procedure was also higher in short DAT group (83.2% versus 75.2% at 5-year, log-rank $P = 0.003$). Even when the analysis was separately performed in patients with paroxysmal AF and those with non-paroxysmal AF, the higher arrhythmia-free rate in the short DAT group remained significant (Supplementary Fig. 3). In the multivariate analysis, short DAT was an independent favorable predictor of recurrent atrial arrhythmias both after the first and second procedures (adjusted hazard ratio [HR] 0.73, 95% confidence interval [CI] 0.61–0.87, $P < 0.001$; adjusted HR 0.74, 95%CI 0.56–0.97, $P = 0.03$, respectively) (Table 2). Other predictors of recurrent atrial arrhythmias were AF type and female gender after the first procedure, and AF type, female gender, CHF, and LA diameter of >50 mm after the second procedure.

3.4. Other clinical outcomes after AF ablation

There were no significant differences between the short and long DAT groups in the 5-year event-free rates from all-cause death, cardiovascular death, heart failure hospitalization, and ischemic stroke (Fig. 2). The event-free rate from cardiovascular hospitalization after the first procedure was significantly higher in short DAT group (61.4% versus 51.8%, log-rank $P = 0.003$). Even when the analysis was separately performed according to AF type, the higher event-free rate from cardiovascular hospitalization in short DAT group remained significant

Table 1
Patient characteristics and procedure characteristics compared between short and long DAT.

	Overall N = 1206	Short DAT N = 675	Long DAT N = 531	*P* value
Age (years) *	64.3 ± 9.5	64.0 ± 9.8	65.5 ± 9.5	0.11
DAT (years) *	2.4 [0.6–6.1]	0.7 [0.3–1.7]	6.9 [4.7–10.2]	<0.001
Paroxysmal atrial fibrillation *	853 (70.7%)	474 (70.2%)	379 (71.4%)	0.66
Previous rhythm control by antiarrhythmic drugs	472 (39.1%)	246 (36.6%)	225 (42.4%)	0.04
Female gender *	350 (29.0%)	193 (28.6%)	157 (29.6%)	0.71
Congestive heart failure *	102 (8.5%)	67 (9.9%)	35 (6.6%)	0.04
Hypertension *	707 (58.6%)	392 (58.1%)	315 (59.3%)	0.66
Diabetes *	195 (16.1%)	109 (16.2%)	86 (16.2%)	0.98
Ischemic stroke/TIA *	119 (9.9%)	49 (7.3%)	70 (13.2%)	<0.001
CHA_2DS_2 score	1.2 ± 1.1	1.1 ± 1.0	1.2 ± 1.1	0.03
CHA_2DS_2-VASc score	2.0 ± 1.5	2.0 ± 1.5	2.1 ± 1.5	0.19
Echocardiography findings				
Left ventricular ejection fraction (%) *	63.1 ± 12.6	63.0 ± 12.3	63.2 ± 13.0	0.75
Left atrial diameter (mm) *	40.9 ± 6.9	40.8 ± 6.7	41.0 ± 7.2	0.61
Procedure characteristics				
Pulmonary veins isolation	1206 (100%)	675 (100%)	531 (100%)	–
Tricuspid valve isthmus ablation	798 (93.6%)	642 (95.1%)	494 (93.0%)	0.13
Superior vena cava isolation	259 (30.4%)	194 (28.7%)	145 (27.3%)	0.58
Complex fractionated atrial electrogram ablation	74 (8.7%)	160 (23.7%)	135 (25.4%)	0.49
Left atrial line ablation	9 (1.1%)	30 (4.4%)	23 (4.3%)	0.92
Medications at discharge				
Oral anticoagulant	1137 (94.3%)	637 (94.4%)	500 (94.2%)	0.88
Antiplatelet therapy	261 (21.6%)	126 (18.7%)	135 (25.4%)	0.005
Antiarrhythmic drugs	97 (8.0%)	43 (6.7%)	54 (10.2%)	0.02
ACE-I/ARB	498 (41.3%)	280 (41.5%)	218 (41.1%)	0.88
Beta blockers	416 (34.5%)	241 (35.7%)	175 (33.0%)	0.32

Continuous variables are presented as mean ± SD or median and interquartile range.
ACE-I = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, DAT = diagnosis-to-ablation time, and TIA = transient ischemic attack.
* Indicated variables incorporated in the multivariable Cox proportional hazard models evaluating the independent risk factors for recurrent atrial tachyarrhythmia.

(Supplementary Fig. 4). The cumulative incidence of OAC discontinuation was also higher in short DAT group (61.5% versus 53.7% at 5-year, log-rank $P = 0.01$) (Supplementary Fig. 5).

Among the 102 patients with prior history of CHF, the 5-year event-free rate from heart failure readmission was significantly higher in short DAT group (85.0% versus 61.0%, log-rank $P = 0.004$), with a relative risk reduction of 61.5%. The event-free rate from ischemic stroke after the first RFCA procedure was extremely high with no significant difference between the groups (98.8% versus 98.6% at 5-year, log-rank $P = 0.60$), even in patients with prior history of ischemic stroke or TIA (97.4% versus 96.1% at 5-year, log-rank $P = 0.66$).

4. Discussion

The current study evaluated the impact of short (<3 years) DAT on the long-term clinical outcomes after RFCA for AF. The main findings of the current study were 1) AF patients with CHF were likely to receive early ablation, while AF patients with prior ischemic stroke or TIA tended to receive delayed ablation; 2) short DAT was associated with higher arrhythmia-free rate after the first and second RFCA procedures, leading to reduced cardiovascular hospitalization; 3) however, PV reconnection rate in patients undergoing second RFCA procedure was comparable between the 2 groups; 4) the long-term clinical outcomes after the first RFCA procedure including all-cause death, cardiovascular death, ischemic stroke or TIA, and heart failure hospitalization were not significantly different between the 2 groups; 5) however, among patients with a past history of CHF or reduced left ventricular function, the risk of heart failure readmission was significantly lower in the short DAT group.

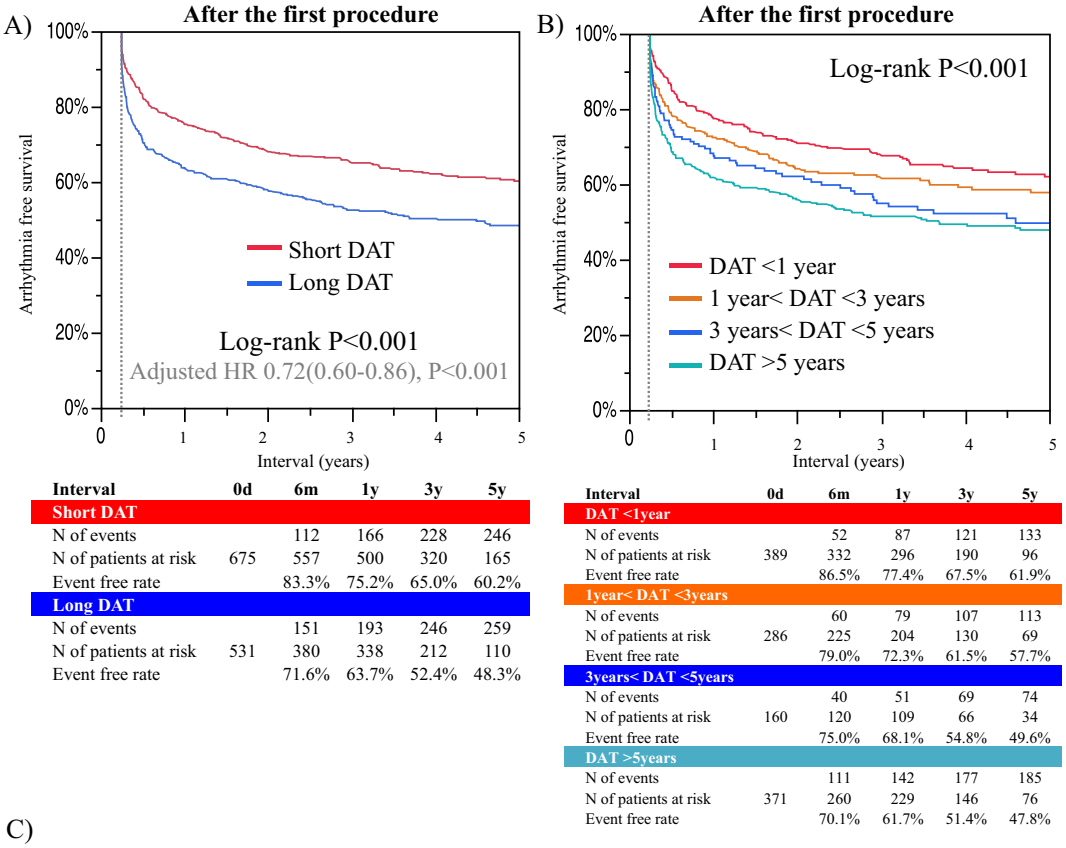
RFCA for AF has been recommended for patients with drug-refractory symptomatic AF [12,13]. However, the timing of RFCA in the management of AF varies among the attending physicians. In the current study, the prevalence of previous rhythm control by AADs was significantly higher in long DAT group, and paroxysmal AF at the first diagnosis had been developed to persistent form of AF during DAT in substantial number of patients. It might suggest that RFCA should be now considered as a first line therapy of paroxysmal AF. The prevalence of prior CHF and ischemic stroke or TIA, known as two major complications of AF, was significantly different between short and long DAT groups. Patients with CHF were likely to receive early RFCA for AF, while patients with prior history of ischemic stroke or TIA were likely to undergo delayed ablation. Possible explanations include the fact that most AF patients with CHF were treated by cardiologists who readily recommend AF ablation, while patients with ischemic stroke or TIA were usually treated by neurologists who are not familiar with AF ablation.

In the current study, ischemic stroke or TIA gradually increased during DAT, and about half the events occurred after diagnosis of AF. The prevalence of stroke or TIA after AF documentation was significantly higher in long DAT group compared with that of short DAT group. OAC had not been administered in about half of such patients, suggesting the underuse of OAC. Needless to say, it is important not only to make an effort to detect AF but also to initiate OAC promptly in patients with documented AF who have thromboembolic risks.

Regarding the elimination of AF, short DAT was associated with significantly lower incidence of arrhythmia recurrence and repeat procedures, which was in accordance with previous reports [14–16]. Our study further evaluated the details of the second RFCA procedures and the impact of short DAT on the arrhythmia-free rate after the second procedure. PV reconnection rate and the prevalence of additional ablation in the second procedures were not significantly different between the groups, but short DAT was associated with higher arrhythmia-free rate even after the second procedure. The higher arrhythmia recurrence rate after the second procedure in the long DAT group might be caused by non-PV foci, because durable PV isolation can be usually achieved by one or two RFCA procedures [18]. Given the lower arrhythmia-free rates after RFCA in the long DAT group regardless of AF type, delayed RFCA with long DAT might accelerate LA degeneration and increase its arrhythmogenicity even in paroxysmal AF.

Our study also addressed the impact of short DAT on the long-term clinical outcomes after RFCA procedure. Although Bunch TJ, et al. previously reported that delays in ablation worsened 1-year outcomes

including death and heart failure [14], there were no significant differences in 5-year clinical outcomes between short and long DAT groups including all-cause and cardiovascular deaths, ischemic stroke, and heart failure hospitalization in the current study. The discordance between the previous and current studies might be due to differences in patient population, follow-up periods, and event rates after RFCA. In the current study, however, shorter DAT was associated with significantly lower incidence of heart failure readmission in patients with a past history CHF at the time of the RFCA. This was presumably due to lower incidence of arrhythmia recurrence in short DAT group. AF and



Interval	0d	6m	1y	3y	5y
Short DAT					
N of events		112	166	228	246
N of patients at risk	675	557	500	320	165
Event free rate		83.3%	75.2%	65.0%	60.2%
Long DAT					
N of events		151	193	246	259
N of patients at risk	531	380	338	212	110
Event free rate		71.6%	63.7%	52.4%	48.3%

Interval	0d	6m	1y	3y	5y
DAT <1year					
N of events		52	87	121	133
N of patients at risk	389	332	296	190	96
Event free rate		86.5%	77.4%	67.5%	61.9%
1year< DAT <3years					
N of events		60	79	107	113
N of patients at risk	286	225	204	130	69
Event free rate		79.0%	72.3%	61.5%	57.7%
3years< DAT <5years					
N of events		40	51	69	74
N of patients at risk	160	120	109	66	34
Event free rate		75.0%	68.1%	54.8%	49.6%
DAT >5years					
N of events		111	142	177	185
N of patients at risk	371	260	229	146	76
Event free rate		70.1%	61.7%	51.4%	47.8%

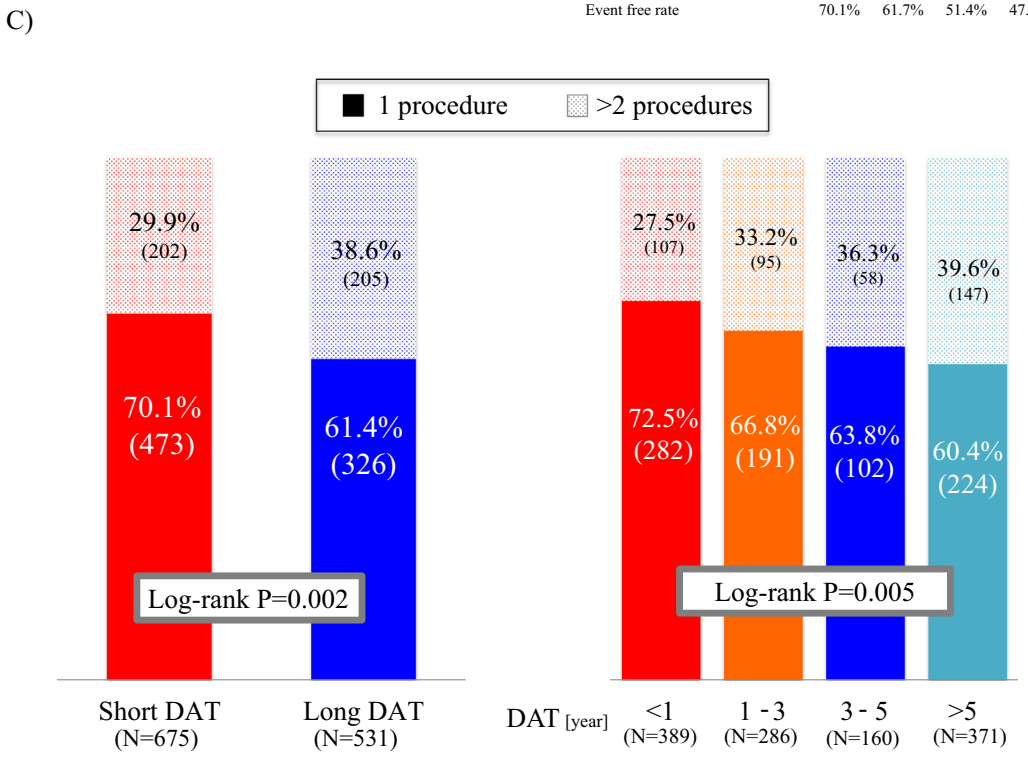
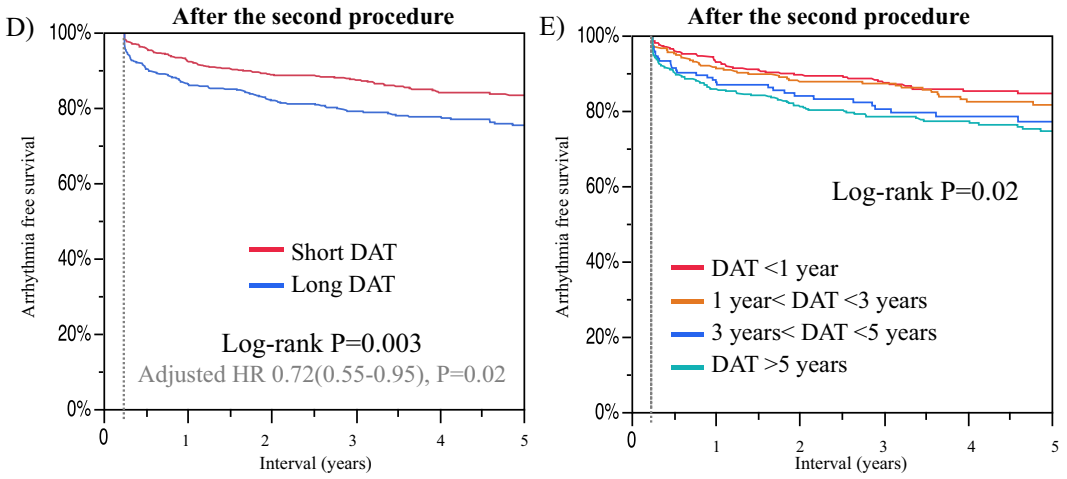


Fig. 1. The event-free survival from recurrent atrial tachyarrhythmias after the first procedure comparing (A) short and long DAT groups, and (B) 4 groups according to DAT duration. (C) The cumulative incidence of repeat ablation procedures. The event-free survival from recurrent atrial tachyarrhythmias after the second procedure comparing (D) short and long DAT groups, and (E) 4 groups according to DAT duration. DAT = diagnosis-to-ablation time.



Interval	0d	6m	1y	3y	5y
Short DAT					
N of events		27	51	80	95
N of patients at risk	675	634	594	399	213
Event free rate		96.0%	97.3%	87.3%	83.2%
Long DAT					
N of events		49	72	106	117
N of patients at risk	531	481	451	299	169
Event free rate		90.8%	86.4%	79.0%	75.2%

Interval	0d	6m	1y	3y	5y
DAT <1year					
N of events		14	27	45	51
N of patients at risk	389	366	343	226	122
Event free rate		96.3%	92.9%	87.3%	84.5%
1year< DAT <3years					
N of events		13	24	35	44
N of patients at risk	286	268	251	173	91
Event free rate		95.4%	91.5%	87.1%	81.5%
3years< DAT <5years					
N of events		14	19	29	32
N of patients at risk	160	146	138	89	48
Event free rate		91.3%	88.1%	80.3%	77.0%
DAT >5years					
N of events		35	53	77	85
N of patients at risk	371	335	313	210	121
Event free rate		90.5%	85.7%	78.4%	74.5%

Fig. 1 (*continued*).

CHF commonly co-exist because one directly predisposes to the other [19]. When both are present, the prognosis is worse than that of either disease alone [19,20].

There are several limitations in the current study. First, the current study was a retrospective observational study. Although short DAT was independently associated with lower arrhythmia-free rates after the first and second RFCA for AF, possibility of unmeasured confounders in the multivariate analyses could not be excluded. Second, although DAT was defined as the time interval from the first diagnosis of AF to the first RFCA procedure, it might be different from "true" AF duration

Table 2
Independent risk factors for recurrent atrial tachyarrhythmia A) after the first procedure, B) after the second procedure.

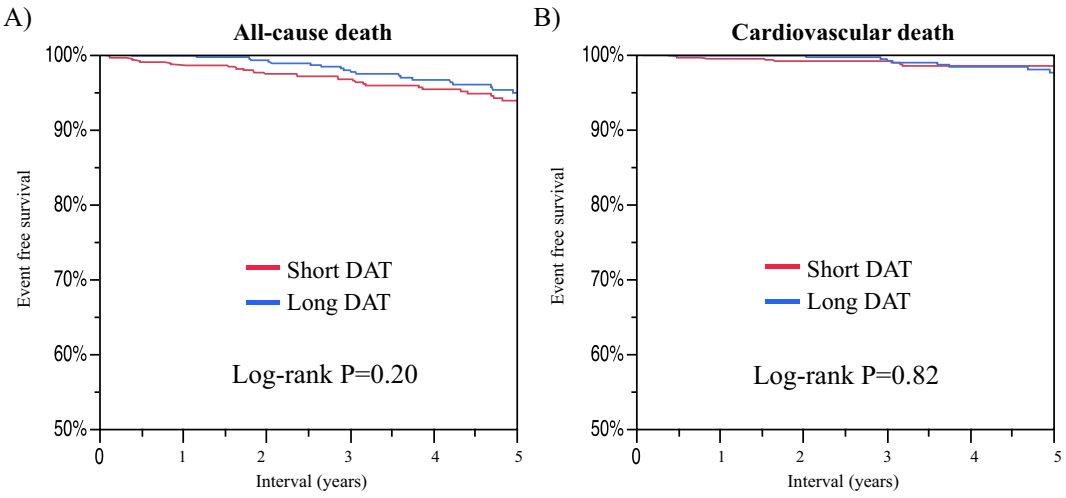
	Univariate		Multivariable	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
A)				
Age ≥ 75 years	1.13 (0.87–1.44)	0.35	1.08 (0.83–1.38)	0.57
Short DAT	0.69 (0.59–0.82)	<0.001	0.72 (0.60–0.86)	<0.001
Persistent AF	1.31 (1.06–1.60)	0.01	1.51 (1.21–1.87)	<0.001
Long-standing AF	2.12 (1.66–2.68)	<0.001	2.12 (1.62–2.73)	<0.001
Female gender	1.18 (0.96–1.39)	0.12	1.26 (1.04–1.52)	0.02
Congestive heart failure	1.48 (1.11–1.94)	0.008	1.30 (0.96–1.75)	0.09
Hypertension	1.17 (0.98–1.40)	0.08	1.13 (0.95–1.36)	0.17
Diabetes	1.05 (0.83–1.31)	0.71	1.04 (0.82–1.31)	0.75
Ischemic stroke/TIA	1.27 (0.97–1.64)	0.08	1.12 (0.85–1.46)	0.41
Left ventricular ejection fraction <40%	1.15 (0.83–1.55)	0.39	0.94 (0.66–1.30)	0.71
Left atrial diameter > 50 mm	1.58 (1.21–2.03)	0.001	1.26 (0.95–1.64)	0.10
B)				
Age ≥ 75 years	1.35 (0.92–1.92)	0.12	1.27 (0.86–1.83)	0.22
Short DAT	0.67 (0.52–0.87)	0.003	0.72 (0.55–0.95)	0.02
Persistent AF	1.48 (1.08–1.99)	0.01	1.84 (1.31–2.56)	<0.001
Long-standing AF	3.19 (2.31–4.32)	<0.001	3.39 (2.36–4.80)	<0.001
Female gender	1.31 (0.99–1.71)	0.06	1.51 (1.13–2.01)	0.006
Congestive heart failure	2.22 (1.51–3.15)	<0.001	1.67 (1.11–2.45)	0.02
Hypertension	1.26 (0.96–1.65)	0.09	1.13 (0.86–1.51)	0.38
Diabetes	1.44 (1.03–1.96)	0.03	1.39 (0.99–1.91)	0.06
Ischemic stroke/TIA	1.33 (0.88–1.93)	0.17	1.12 (0.74–1.63)	0.59
Left ventricular ejection fraction <40%	1.11 (0.67–1.73)	0.67	0.78 (0.46–1.25)	0.32
Left atrial diameter > 50 mm	2.67 (1.89–3.68)	<0.001	1.83 (1.27–2.59)	0.002

AF = atrial fibrillation, CI = confidence interval, DAT = diagnosis-to-ablation time, and HR = hazard ratio, HR = hazard ratio and TIA = transient ischemic attack.

in asymptomatic patients. Finally, we might have underestimated the incidence of recurrent atrial tachyarrhythmias after RFCA because they were evaluated only by occasional 12 lead ECG and periodical Holter monitoring in the current study.

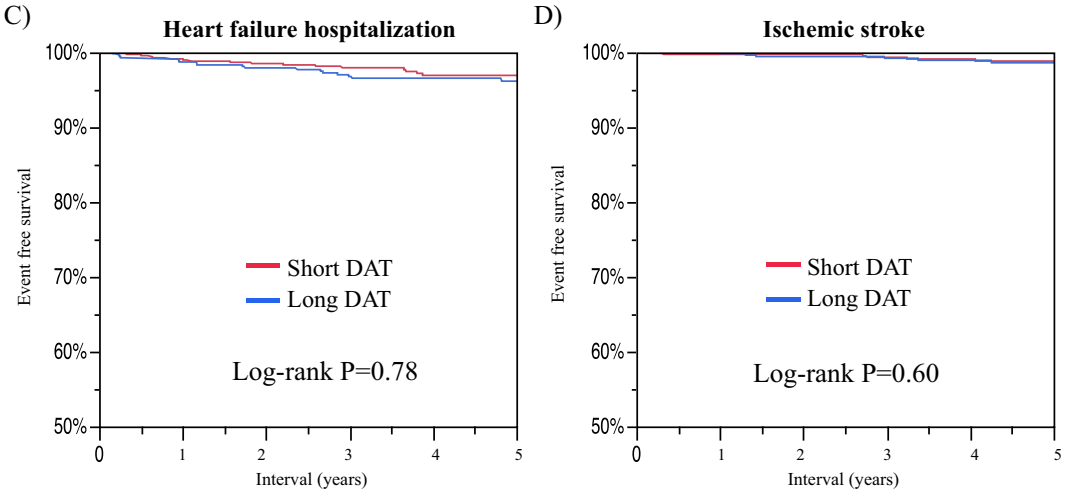
5. Conclusion

In the management of AF, early RFCA was associated with significantly lower arrhythmia recurrence compared with delayed RFCA,



Interval	0d	6m	1y	3y	5y
Short DAT					
N of events		7	10	21	32
N of patients at risk	675	668	664	490	274
Event free rate		99.0%	98.5%	96.7%	93.8%
Long DAT					
N of events		1	1	10	20
N of patients at risk	531	530	530	418	241
Event free rate		99.8%	99.8%	97.9%	94.9%

Interval	0d	6m	1y	3y	5y
Short DAT					
N of events		3	4	6	9
N of patients at risk	675	668	664	490	274
Event free rate		99.6%	99.4%	99.1%	98.4%
Long DAT					
N of events		1	1	3	9
N of patients at risk	531	530	530	418	241
Event free rate		99.8%	99.8%	99.4%	97.6%

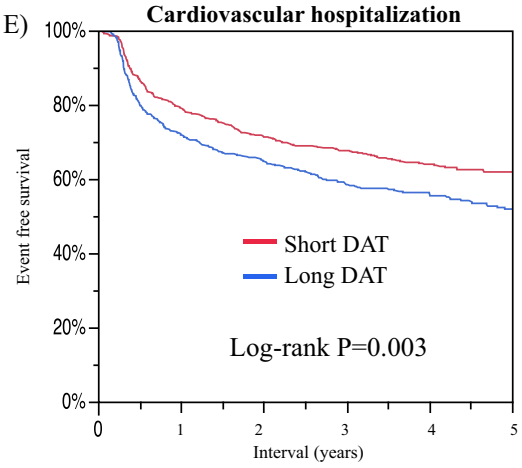


Interval	0d	6m	1y	3y	5y
Short DAT					
N of events		2	6	13	17
N of patients at risk	675	666	669	480	270
Event free rate		99.7%	99.1%	97.9%	96.9%
Long DAT					
N of events		5	7	16	18
N of patients at risk	531	526	524	408	236
Event free rate		99.1%	98.7%	96.8%	96.1%

Interval	0d	6m	1y	3y	5y
Short DAT					
N of events		2	2	4	6
N of patients at risk	675	666	662	487	270
Event free rate		99.7%	99.7%	99.3%	98.8%
Long DAT					
N of events		0	0	4	6
N of patients at risk	531	530	530	415	240
Event free rate		100%	100%	99.2%	98.6%

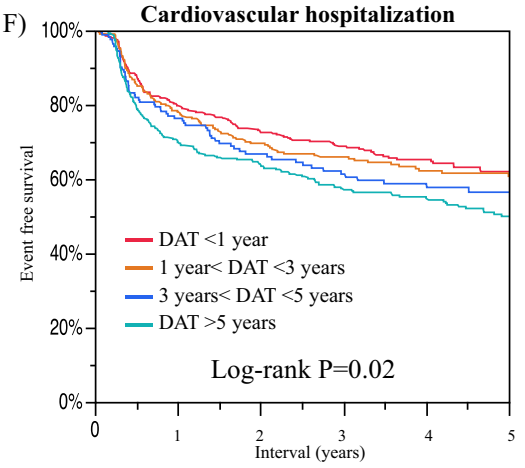
Fig. 2. The event-free survival in the entire study population from (A) all-cause death, (B) cardiovascular death, (C) heart failure hospitalization, and (D) ischemic stroke, comparing short and long DAT groups. The event-free survival in the subgroup of patients from cardiovascular hospitalization, comparing (E) short and long DAT groups, and (F) 4 groups according to DAT duration. The event-free survival from heart failure readmission in the subgroup of patients with prior CHF, comparing (G) short and long DAT groups, and (H) 4 groups according to DAT duration. (I) The event-free survival from recurrent ischemic stroke in the subgroup of patients with prior history of ischemic stroke or TIA. DAT = diagnosis-to-ablation time, CHF = congestive heart failure, and TIA = transient ischemic attack.

E)



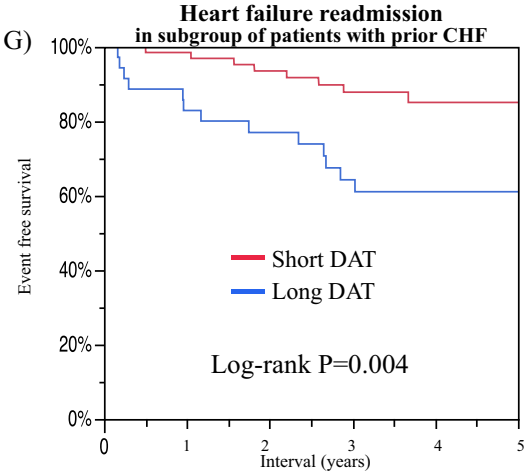
Interval	0d	6m	1y	3y	5y
Short DAT					
N of events		89	142	213	237
N of patients at risk	675	587	532	344	172
Event free rate		86.8%	79.0%	67.5%	61.4%
Long DAT					
N of events		103	150	214	235
N of patients at risk	531	428	381	244	123
Event free rate		80.6%	71.8%	58.4%	51.8%

F)



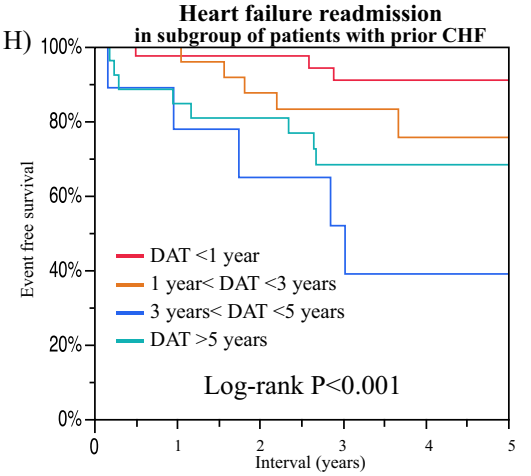
Interval	0d	6m	1y	3y	5y
DAT <1year					
N of events		47	79	118	133
N of patients at risk	389	342	309	200	96
Event free rate		87.9%	79.7%	68.7%	61.9%
1year< DAT <3years					
N of events		42	63	95	104
N of patients at risk	286	245	223	144	76
Event free rate		85.3%	78.0%	65.9%	60.7%
3years< DAT <5years					
N of events		29	38	59	64
N of patients at risk	160	131	122	75	37
Event free rate		81.9%	76.3%	61.3%	56.4%
DAT >5years					
N of events		74	112	155	171
N of patients at risk	371	297	259	169	86
Event free rate		80.1%	69.8%	57.1%	49.9%

G)



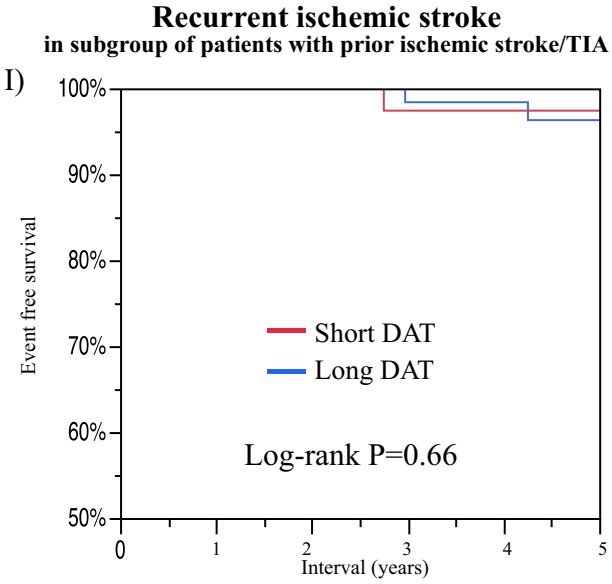
Interval	0d	6m	1y	3y	5y
Short DAT					
N of events		0	1	7	8
N of patients at risk	67	64	62	43	20
Event free rate		100%	98.4%	87.7%	85.0%
Long DAT					
N of events		4	6	12	13
N of patients at risk	35	31	29	20	8
Event free rate		88.6%	82.9%	64.2%	61.0%

H)



Interval	0d	6m	1y	3y	5y
DAT <1year					
N of events		0	1	3	3
N of patients at risk	42	39	38	28	12
Event free rate		100%	97.4%	90.9%	90.9%
1year< DAT <3years					
N of events		0	0	4	5
N of patients at risk	25	25	24	15	8
Event free rate		100%	100%	83.1%	75.6%
3years< DAT <5years					
N of events		1	2	4	5
N of patients at risk	9	9	7	4	1
Event free rate		88.9%	77.8%	51.9%	38.9%
DAT >5years					
N of events		3	4	8	8
N of patients at risk	26	23	22	16	7
Event free rate		88.5%	84.6%	68.2%	68.2%

Fig. 2 (*continued*).



Interval	0d	6m	1y	3y	5y
Short DAT					
N of events		0	0	1	1
N of patients at risk	49	49	49	36	18
Event free rate		100%	100%	97.4%	97.4%
Long DAT					
N of events		0	0	1	2
N of patients at risk	70	70	70	58	38
Event free rate		100%	100%	98.3%	96.1%

Fig. 2 (*continued*).

leading to reduced cardiovascular hospitalization, especially in heart failure patients.

Conflicts of interest

None.

Source of funding

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.03.036.

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