Redefining the Blanking Period by a Long-Term Follow-Up after Atrial Fibrillation Ablation Using Second-Generation Cryoballoon

Yu Xia,¹ MD, Jun Liu,¹ MD, Yuhe Jia,¹ MD, Hao Zhang,² MD, Miao Yu,¹ MD, Xiaofeng Li,¹ MD and Pihua Fang,¹ MD

Summary

On the basis of radiofrequency ablation of atrial fibrillation (AF), some studies suggested that early recurrences of atrial tachyarrhythmia (ERATs) were associated with late AF recurrence (LAFR), and some also suspected and challenged the current recommended 90 day blanking period. We aim to evaluate the impact of ERAT on long-term success and to determine the optimum blanking period after AF ablation using second-generation cryoballoon (sg-CB). From August 2016 to October 2018, 369 consecutive patients who successfully underwent initial AF ablation using sg-CB at the Fuwai Hospital were finally enrolled. All patients were followed up no less than 12 months. Receiver operating characteristic curve analysis was used to determine the optimum blanking period after AF ablation. There were 62 (16.8%) who experienced ERAT. After a median follow-up of 615 days, 74.5% were free of LAFR after the 90 day blanking period. Incidence of freedom from LAFR during the long-term follow-up was markedly lower in patients with ERAT than in those without ERAT (27.4% versus 84.0%; log-rank $P < 0.001$). Furthermore, only ERAT (HR 8.579; 95% CI 5.604-13.133; $P < 0.001$) was significantly associated with an increased risk of LAFR after adjusting for other factors. The optimum cut-off time point for the blanking period was 21.5 days (sensitivity: 71.1%, specificity: 94.1%). In conclusion, ERAT was an independent predictor of LAFR after AF ablation using sg-CB. Based on our findings, blanking period was advised to be shortened to 21.5 days or about 3 weeks instead of 90 days after CB ablation.

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Key words: Arrhythmia, Pulmonary vein isolation, Early recurrence, Electrocardiogram

Catheter ablation based on pulmonary vein isolation (PVI) is an effective treatment option for patients affected by symptomatic atrial fibrillation (AF) in whom antiarrhythmic drugs are ineffective or not tolerated.^{1,2} Presently, expert consensus recommends that a blanking period of first 90 days following the procedure should not be considered when evaluating AF recurrence, given the fact that up to half of the patients with early recurrences of atrial tachyarrhythmia (ERAT) would not experience late AF recurrence (LAFR) after blanking period.^{1,3} This blanking period is defined as a period of time post-ablation during which any recurrence of AF, atrial flutter (AFL), or atrial tachycardia (AT) is not considered as ablation failure.

However, ERATs after initially successful PVI within the blanking period are not scarce, with a pooled estimated incidence of 37.8%.⁴ Additionally, the long-term clinical significance of these ERAT remains unclear. Recently, an increasing number of studies based on radiofre-

quency (RF) ablation of AF have reported that ERAT was strongly associated with LAFR, especially if ERAT occurred in the late blanking period.⁵⁻⁹ Furthermore, based on their studies on RF ablation of AF, some researchers suggested that the time of the blanking period should be shortened to yield more accurate determination and intervention for the recurrence of AF.

Unfortunately, evidence on the long-term clinical significance of ERAT after AF ablation using second-generation cryoballoon (sg-CB) and recommendation for its relevant blanking period is limited. We aim to evaluate the impact of ERAT on the long-term success and to determine the optimum blanking period after successful PVI using sg-CB.

Methods

Study population: From August 2016 to October 2018, all consecutive patients who underwent PVI as the initial

From the ¹State Key Laboratory of Cardiovascular Disease, Cardiac Arrhythmia Center, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China and ²Department of Cardiology, Chongqing General Hospital, Chongqing, China.

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Address for correspondence: Pihua Fang, MD or Xiaofeng Li, MD, State Key Laboratory of Cardiovascular Disease, Cardiac Arrhythmia Center, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, No.167 North Lishi Road, Xicheng District, Beijing, 10037, China. E-mail: fangph@vip.sina.com or lixiaofengfw@aliyun.com

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Figure 1. Flow chart of study participants included and excluded in the study.

procedure using sg-CB ablation at the Fuwai Hospital for documented symptomatic and drug refractory (failure of ≥ 1 class I or III antiarrhythmic drugs) AF were considered for our retrospective observational analysis. Exclusion criteria are as follows: 1) patients with acute thrombosis (including myocardial infarction and stroke) or severe bleeding occurred within 8 weeks before the procedure; 2) those with heart valve disease; 3) those who concomitantly underwent left atrial appendage occlusion; 4) those with other procedure contraindications such as severe anemia and liver and kidney dysfunction; 5) those with previous ablation of AF; and 6) those who could not provide informed consent. As shown in Figure 1, we screened 432 patients during the study period, and 369 patients with AF were finally recruited in our analysis. All enrolled patients gave written consent for data collection and publication. The present study was conducted accord-

ing to the ethical principles for medical research involving human subjects established by the Declaration of Helsinki, protecting the privacy of all participants as well as the confidentiality of their personal information.

Preprocedural management: Preoperative routine laboratory examinations were completed within 1 week before ablation. Meanwhile, the function and structure of the heart, including left atrial diameter, left ventricular end-diastolic diameter, and left ventricular ejection fraction, were evaluated by echocardiography. Transesophageal echocardiography was performed before the day of the procedure to ensure the absence of intracardiac thrombi. All patients underwent a preprocedural computed tomographic scan to evaluate the detailed anatomy of the left atrium and pulmonary vein (PV). Patients were prescribed with oral anticoagulation agents (OCAs) at least 3 weeks before the procedure. Patients who were taking

warfarin discontinued this medication 2 days before the procedure, and low molecular-weight heparin (LMWH) was injected subcutaneously for bridging anticoagulation and one dose of LMWH was discontinued in the early morning of the operation day. Patients who were taking novel oral anticoagulant drugs discontinued taking them only once in the early morning of the operation day. All antiarrhythmic drugs (AADs) were discontinued at least 3 days before the procedure except β -blocker.

Cryoballoon ablation procedure: The ablation procedure was conducted as previously reported.^{10,11} Briefly, all procedures were conducted under local anesthesia. A decapolar catheter (St. Jude Medical Inc., MN, or C. R. Bard, Inc., NY) was placed in coronary sinus via right internal jugular vein to record the potential of atria and ventricles, and a bipolar catheter (St. Jude Medical Inc., MN) was placed in right ventricular apex via right femoral vein to ventricular standby pacing in case of bradycardia caused by vagal reflex. A single transseptal puncture using 8.5 Fr SL1 atrial septal puncture sheath (Synaptic Medical Inc., Beijing) was conducted via right femoral venous approach guided by fluoroscopy. After obtaining LA access, a 100 IU/kg heparin was given through peripheral vein. Thereafter, activated clotting time was maintained 250-350 seconds by supplementing heparin depending on the results of testing every 15-30 minutes.

Selective angiography was used to confirm the PV anatomy. Then, a 15-Fr steerable sheath (FlexCath Advance, Medtronic Inc., MN) was exchanged with a stiff guidewire and inserted into the left atrium. A second-generation 28 mm cryoballoon (Arctic Front, Medtronic Inc.) with a 15 mm octapolar circular mapping catheter (Achieve, Medtronic Inc., MN) was advanced into each PV ostium. Once completed occlusion was achieved, cryothermal energy was started. Each cryoenergy application was delivered for 180 seconds. Conventionally, the left superior PV (LSPV) was ablated first, followed by the left inferior PV (LIPV), right inferior PV (RIPV), and right superior PV (RSPV). PV potential was recorded with the Achieve at a proximal site within the ostium before ablation in each vein. Additional cryoenergy applications were not applied if the veins were isolated. Before the ablation of right-sided PVs, the bipolar catheter was removed from right ventricular apex to the posterior wall of superior vena cava near the right subclavian vein to pace the right phrenic nerve (10-20 mA at 2.0 ms pulse width at a 1200 ms cycle length) during the ablation of right-sided PVs. Any sign of diminished diaphragmatic contractions initiated an immediate cryoablation termination as described by Ghosh, *et al.*¹² The procedural endpoint of cryoablation was confirmed as bi-directional blockage of each PV. Drug cardioversion by ibutilide was used to terminate AF in patients who did not achieve sinus rhythm after PVI, whereas direct current cardioversion was used if patients were with organic cardiomyopathy, severe cardiac insufficiency, or ineffective to drug cardioversion.

Post-ablation management: Echocardiography was performed within 3 hours after the procedure to exclude pericardial effusion, and electrocardiographic (ECG) telemetry was continuously monitored for at least 24 hours for arrhythmia in all patients. Patients were discharged the sec-

ond day after the procedure if their clinical status was stable. OCAs were restarted the same evening of the ablation and continued for at least 3 months. Further use of OACs was determined by their CHA₂DS₂-VASc scores.²⁾ Patients who were taking AADs before the procedure resumed taking them for the first 3 months after the procedure, and AADs were ceased if the patient was free of AF relapse.

Follow-up: All patients were followed up closely after the procedure for no less than 12 months unless they experienced LAFR. A 24 hour Holter monitor and in-office ECG were performed at the 1st-, 3rd-, 6th-, 9th-, and 12 th-month scheduled follow-up visits and every 6 months thereafter. Furthermore, patients with any suspicious symptom of AF would be asked to undergo ECG and 24 hour Holter monitor immediately in hospital, and they were further evaluated the recurrence of AF. ERAT was defined as an episode of sustained AF, AFL, or AT of 30 seconds within 90 days (blanking period) after the initial ablation procedure. LAFR was defined as any documented atrial tachyarrhythmia (AF, AFL, or AT) lasting at least 30 seconds after blanking period.

Statistical analysis: Kolmogorov-Smirnov test was used to estimate the normality of each continuous variable. Continuous variables were expressed as means $\pm$ standard deviation if there were no significant deviation from the normal distribution or reported as median and quartile. Categorical variables were reported as counts (percentage). Continuous variables with normal distribution were analyzed by independent sample *t*-test, whereas those of non-normal distribution were analyzed by Mann-Whitney *U*-test. Categorical variables were compared using the chi-square test or the Fisher exact test, as appropriate. Event-free survival was estimated using the Kaplan-Meier method and compared using the log-rank test. Predictors of LAFR were analyzed using Cox proportional hazards regression models. A receiver operator characteristic (ROC) curve analysis was conducted to determine the accurate cut-off time point of ERAT for LAFR. *P*-values less than 0.05 were considered statistically significant, and all tests were two-tailed. All statistical analyses were conducted by using SPSS 22.0 (SPSS Inc., Chicago, IL, USA), and figures were drawn by using GraphPad Prism 8.0 (GraphPad Software, San Diego, CA, USA).

Results

Baseline population characteristics: The detail characteristics of the patients at baseline are shown in Table I. Study participants included a total of 369 AF patients, 123 (33.3%) of whom were female and 98 (26.6%) of whom were non-paroxysmal AF (NPAF). The mean age of the patients was 59.0 $\pm$ 9.8 years. The mean CHA₂DS₂-VASc and HASBLED scores were 2.1 $\pm$ 1.5 and 1.4 $\pm$ 1.0, respectively. Generally, 62 (16.8%) patients experienced ERAT within the 90 day blanking period, of which nine patients (14.5%) were asymptomatic and 53 patients (85.5%) were symptomatic. Except for a higher prevalence of NPAF (37.1% versus 24.4%; *P* < 0.05) in the ERAT group than in the non-ERAT group, no other clinically relevant difference has been shown between the two groups at baseline.

Table I. Baseline Characteristics of Patients with and without ERAT

	Total (<i>n</i> = 369)	ERAT group (<i>n</i> = 62)	Non-ERAT group (<i>n</i> = 307)	<i>P</i> -value
Female	123 (33.3)	20 (32.3)	103 (33.6)	0.844
Hypertension	213 (57.7)	40 (64.5)	173 (56.4)	0.235
DM	75 (20.3)	15 (24.2)	60 (19.5)	0.407
TIA/stroke	51 (13.8)	9 (14.5)	42 (13.7)	0.862
CHF	27 (7.3)	3 (4.8)	24 (7.8)	0.594
PVD	89 (24.1)	11 (17.7)	78 (25.4)	0.198
CHD	96 (26.0)	21 (33.9)	75 (24.4)	0.122
NPAF	98 (26.6)	23 (37.1)	75 (24.4)	0.039
Age (years)	59.0 ± 9.8	61.2 ± 11.8	58.5 ± 9.3	0.053
BMI (kg/m ²)	26.0 ± 3.5	25.8 ± 3.1	26.0 ± 3.6	0.653
LAD (mm)	39.0 ± 5.0	39.7 ± 5.2	38.9 ± 4.9	0.237
LVEDD (mm)	47.7 ± 4.1	47.6 ± 4.4	47.7 ± 4.0	0.914
LVEF (%)	63.1 ± 4.9	62.4 ± 6.1	63.2 ± 4.6	0.235
CHA ₂ DS ₂ -VASc	2.1 ± 1.5	2.2 ± 1.7	2.0 ± 1.5	0.344
HASBLED	1.4 ± 1.0	1.6 ± 1.1	1.4 ± 1.0	0.155

Data are expressed as $\bar{x} \pm s$ or *n* (%). ERAT indicates early recurrences of atrial tachyarrhythmia; DM, diabetes mellitus; TIA, transient ischemic attack; CHF, chronic congestive heart failure; PVD, peripheral vascular diseases; CHD, coronary heart diseases; NPAF, non-paroxysmal atrial fibrillation; LAD, left atrial diameter; LVEDD, left ventricular end-diastolic diameter; and LVEF, left ventricular ejection fraction.

Figure 2. Kaplan-Meier curves showing time to freedom of late atrial fibrillation recurrence (LAFR) after the 90 day blanking period in patients with and without early recurrences of atrial tachyarrhythmia (ERAT) after atrial fibrillation ablation.

Prevalence and associated factors of LAFR: After a median follow-up period of 615 [415, 822.5] days, a total 275 out of 369 patients (74.5%) were free of LAFR after the 90 day blanking period. Kaplan-Meier curves showed that percentage of freedom from LAFR during the follow-up was significantly lower in patients with ERAT group (17/62) than in those without ERAT (258/307) (27.4% versus 84.0%; log-rank $P < 0.001$; Figure 2).

As shown in Table II, univariate Cox regression analysis indicated that NPAF (HR 1.707, 95% CI 1.123-2.594, $P < 0.05$) and ERAT (HR 9.087; 95% CI 6.019-13.718; $P < 0.001$) were significantly associated with an increased risk of LAFR. Subsequently, variables with a P -value less than 0.10 in the univariate Cox regression analysis were included in the multivariable Cox regression analysis. Multivariate Cox regression analysis showed that only ERAT (HR 8.579; 95% CI 5.604-13.133; $P < 0.001$)

was significantly and independently associated with an increased risk of LAFR after adjusting for coronary heart diseases (CHD) and NPAF (Table II).

The optimal cut-off time point for the blanking period after ablation of AF: The impact of the time of ERAT during the 90 day blanking period on the incidence of LAFR was further studied. Timing of ERAT during the blanking period was significantly later in patients with LAFR than in those without LAFR (33 [16.5, 61] versus 7 [5, 15.5]; $P < 0.01$; Figure 3). Interestingly, recurrences of AF confined in the blanking period occurred almost within 1 month after ablation. However, once ERAT occurred in the latter 2 months of blanking period, patients would experience later relapse and were confirmed with LAFR (Figure 3).

ROC curve analysis was performed to determine the accurate cut-off time point of ERAT for LAFR to better define the blanking period after ablation procedure. As shown in Figure 4, the optimal cut-off time point for the blanking period was 21.5 days with area under the curve (AUC) of 0.824 (95% CI 0.716-0.932), along with sensitivity and specificity of 71.1% and 94.1%, respectively.

The findings of the repeat ablation: There were 13 patients underwent repeat ablation, which was conducted with RF irrigated-tip catheter guided by contact force monitoring using CARTO 3 (Biosense Webster) three-dimensional electroanatomic mapping system after a median time of 337 [163.5, 569.5] days from the initial procedure. In these 13 patients, seven (53.8%) experienced ERAT, of whom five had PV reconnection; six (46.2%) did not experience ERAT, of whom five had PV reconnection. Particularly, four (80%) patients with PV reconnection and ERAT developed ERAT 3 weeks after the initial ablation. Of all 57 PVs in the 13 patients, 17 (29.8%) showed PV reconnection in 10 patients (1.7 PV reconnections per patient) at the time of the repeat ablation procedure. In 17 reconnecting veins, 11 (64.7%) were right-

Table II. Univariate and Multivariate Cox Regression Analysis for LAFR

	Uni-COX analysis		Multi-COX analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Sex	1.118 (0.732-1.707)	0.607		
Hypertension	1.031 (0.684-1.552)	0.885		
DM	0.968 (0.579-1.618)	0.900		
TIA/stroke	1.374 (0.802-2.355)	0.248		
CHF	1.145 (0.554-2.365)	0.714		
PVD	1.045 (0.647-1.688)	0.857		
CHD	1.505 (0.978-2.314)	0.063	1.167 (0.755-1.803)	0.487
NPAF	1.707 (1.123-2.594)	0.012	1.190 (0.774-1.829)	0.428
Age (years)	1.000 (0.979-1.022)	0.970		
BMI (kg/m ²)	1.005 (0.949-1.064)	0.866		
LAD (mm)	1.034 (0.993-1.077)	0.108		
LVEDD (mm)	0.995 (0.946-1.045)	0.829		
LVEF (%)	1.017 (0.974-1.062)	0.444		
ERAT	9.087 (6.019-13.718)	< 0.001	8.579 (5.604 -13.133)	< 0.001

LAFR indicates late atrial fibrillation recurrence. Other abbreviations the same as in Table I.

Figure 3. The difference timing of early recurrences of atrial tachyarrhythmia (ERAT) between patients with and without late atrial fibrillation recurrence (LAFR).

sided PVs (five RSPVs and six RIPVs), whereas six (35.3%) were left-sided PVs. Repeat PV isolation and substrate ablation procedures were successfully performed in all patients. In a mean follow-up of 374.2 ± 197.9 days after repeat procedure, two of 13 (15.4%) continued to experience AFL.

Discussion

The main findings of the present study are summarized as follows: (1) The incidence of ERAT within the 90 day blanking period after sg-CB ablation procedure was

16.8% in the present study population; (2) ERAT was an independent predictor of LAFR; (3) timing of ERAT during the blanking period in patients with LAFR was significantly later than in patients without LAFR; and (4) the ideal cut-off point for the blanking period was 21.5 days with sensitivity and specificity of 71.1% and 94.1%, respectively.

To our best knowledge, the study has the biggest sample and the longest follow-up period so far to redefine the blanking period after AF ablation using sg-CB. ERAT occurring during the blanking period after AF ablation procedure is a common phenomenon. The pooled analysis

Figure 4. Receiver operating characteristic curve analysis for defining the optimal cut-off time point for the blanking period after ablation of atrial fibrillation.

of Andrade demonstrated that ERAT rates after AF ablation using a conventional point-by-point RF technique ranged from 16% to 67% with a pooled estimate of approximately 38%.^{4,5,8)} Similarly, previous studies have reported that the incidence of ERAT after CB ablation occurred over a range of 8.8% to 51.5% in patients due to varying detecting means during follow-up.^{7-10,13,14)} The most reliable study using continuous cardiac monitoring by implantable loop recorder after CB ablation reported the incidence of ERAT was 28%.⁷⁾ In the present study, 16.8% of patients experienced ERAT after sg-CB ablation, consistent with previous studies.

According to current expert consensuses, ERAT in the blanking period should not be considered as a failure of ablation. However, increasing evidences have shown that the ERAT is a strong independent predictor of LAFR and long-term ablation failure.⁵⁻¹⁰⁾ Mugnai, *et al.*¹⁰⁾ reported that ERAT was strongly associated with LAFR after paroxysmal AF ablation using sg-CB ablation (HR 6.79; 95% CI 3.52-10.14; $P < 0.0001$). Furthermore, their study reported that ERAT after ablation significantly increased the risk of LAFR and all patients who experienced ERAT in the latter half of the blanking period would have LAFR. Pieragnoli, *et al.*⁷⁾ evaluated the role of ERAT in predicting failure at the 12th-month post-ablation by examining 60 consecutive patients with paroxysmal and persistent/longstanding persistent AF who underwent ablation using first- or second-generation cryoballoon. They found that NPAF (HR 3.113; 95% CI 1.309-7.403; $P = 0.010$) and ERAT (HR 3.453; 95% CI 1.544-7.722; $P = 0.003$) were independent predictors of LAFR. Moreover, our results showed that incident rate of freedom from LAFR during the long-term follow-up was markedly lower in patients with ERAT than in those without ERAT (27.4% versus 84.0%, respectively; log-rank $P < 0.001$;

Figure 2). Furthermore, only ERAT (HR 8.579; 95% CI 5.604-13.133; $P < 0.001$) was significantly and independently associated with an increased risk of LAFR after adjusting for CHD and NPAF (Table II).

The concept of a blanking period is based on the assumption that the mechanism of ERAT (which do not necessarily represent treatment failure) probably differs from that of LAFR after ablation of AF. LAFRs are more likely due to chronic reconnection of previously isolated PV, as well as the development of late macroreentry organized AT related to gaps in additional ablation lines.^{15,16)} Conversely, potential mechanisms of ERAT include arrhythmia caused by prolongation in action potential duration of atrial myocardium due to inflammation and tissue edema after ablation, arrhythmia triggered by a temporary imbalance of autonomic nerve tension, reentrant arrhythmia mediated by slow conduction of scar tissue, recovery of PV conduction caused by incomplete ablation, absence of unabiding ablation injury or incomplete blockade of the target area, and presence of other uninterrupted lesions (e. g., superior vena cava and Marshall ligament).¹⁷⁻²¹⁾ We found that 71.4% of patients who experienced ERAT had PV reconnection during the repeat ablation. Moreover, 80% of patients with PV reconnection and ERAT developed ERAT 3 weeks after the initial ablation. Consequently, among patients with ERAT in the blanking period, some are probably ascribed to the chronic reconnection of PV.

The timing of ERAT may have implications for the underlying arrhythmia mechanism. We observed a phenomenon that almost all patients with ERAT in the latter 2 months of blanking period would experience LAFR, which was in parallel with Mugnai, *et al.*'s. By investigating the relationship between the time of ERAT and PV reconnection at mandatory repeat electrophysiology study 2 months after PVI, Das, *et al.* found that ERAT beyond 4 weeks after PVI was strongly associated with PV reconnection, whereas ERAT confined to the first month was unrelated to underlying PV reconnection.²²⁾ Another study conducted by Liang, *et al.* revealed that ERAT occurring in the initial 2 weeks following PVI may be related to transient post-ablation inflammation.²³⁾ Additionally, tissue edema of left atrium could occur immediately after AF ablation and resolve within 1 month, and transient ERAT may be induced by the edema during such period.²⁴⁻²⁶⁾ Therefore, we speculate that patients with ERAT in the latter 2 months of blanking period in the present study highly possibly experience the PV reconnection other than transient post-ablation inflammatory reaction or tissue edema.

Thus far, expert consensuses still recommend a blanking period of first 90 day following the AF ablation, because one-third to half of patients with ERAT remain free of AF during long-term follow-up. Even so, some researchers challenge the conventional 90 day blanking period. Alipour, *et al.*⁹⁾ have reported that 23 days after PVI using RF was the ideal period of time for the blanking period (AUC 0.70; sensitivity 69.2%; specificity 61.2%; $P < 0.001$). In the ADVANCE trial, the optimal cut-off time point of blanking time for yielding the greatest discriminatory potential was 50 days (AUC 0.8218; $P < 0.0001$).²⁷⁾

Based on the results that all patients with ERAT in the latter half of blanking period were confirmed as definitive recurrences, rather than the results that the cut-off time point of blanking period was determined by ROC analysis, Mugnai, *et al.*¹⁰⁾ suggested that blanking period should be shortened to 1.5 months in patients with paroxysmal AF after PVI using sg-CB. Similarly, shorter time of the blanking period than that recommended by expert consensus was also observed in the present study, and the optimal cut-off time point for the blanking period predicting LAFR was 21.5 days post-ablation with AUC of 0.824 (95% CI 0.716-0.932; $P < 0.01$), along with a sensitivity of 71.1% and a specificity of 94.1% (Figure 4). Thus, we suggested a shorter blanking period after sg-CB ablation with 21.5 days or 3 weeks instead of 90 days. Shortening the blanking period to 3 weeks will contribute to the further management of patients with ERAT occurring 3 weeks after the procedure. According to the current recommendation, patients who experienced ERAT between 3 weeks and 90 days after the procedure would not be treated with comprehensive management for AF between 90 days after the procedure and LAFR. However, structural, electrical, and mechanical remodeling of the atria might promote AF-induced progression during this period, and further resulted in poor clinical outcomes.^{17,28)} Our findings indicated that patients should be treated with relative management in such period for more clinical benefits. Previous studies found that patients who underwent electrical cardioversion for ERAT 1 month post-ablation procedure still had a quite high incidence of LAFR, and those patients still required a repeat ablation procedure.^{29,30)} It was reported that patients who underwent early re-ablation within the blanking period for ERAT had a significantly lower rate of LAFR,³¹⁾ and patients who experienced ERAT after the 15th day of blanking period should undergo repeat ablation procedure.³²⁾ As we discussed above, we speculated that AF recurrence in months 2 and 3 after the procedure was more likely related to PV reconnection. Therefore, those patients should undergo repeat ablation procedure besides cardioversion. Certainly, clinical feasibility and patients' condition should be prudently evaluated when a repeat ablation procedure within is being performed in a short time, and the confirmation for the exact time of repeat ablation procedure still need further study and more clinical data. Moreover, caution should be taken when generalizing our findings to clinical practice, and further large-scale prospective randomized studies are warranted to confirm our findings.

Limitations: There are several limitations in our research. First, the present study is a single-centered and retrospective observational investigation. Therefore, the conclusion slightly lacks clinical convincingness. Second, the diagnostic protocol adopted during follow-up did not include intensive monitoring by continuous transtelephonic monitoring or implantable loop recorder. Therefore, asymptomatic episodes of AF could be unrecognized during the whole follow-up period, especially during the blanking period. Thereupon then the incidence of ERAT and LAFR could be underestimated. Third, the recommended blanking period in the present study was based on a statistical concept. Further investigation should be conducted to de-

termine the optimal blanking period by evaluating the clinical benefit of different re-ablation time for patients who are experiencing ERAT. Finally, the mechanisms and potential treatment of ERAT had not been investigated in the present study, which also needs further investigation.

Conclusion

The results of the present study showed that ERAT occurring within the blanking period was common, with an incidence rate of 16.8%. ERAT was an independent predictor of LAFR after AF ablation using sg-CB (HR 8.579; 95% CI 5.604-13.133; $P < 0.001$). Based on the findings of the present study, the blanking period was recommended to be shortened to 21.5 days or about 3 weeks instead of 90 days after CB ablation, which would require further large-scale prospective randomized studies to be adequately validated before being applied to clinical practice.

Disclosure

Conflicts of interest: The authors declare no conflict of interest.

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