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MINIREVIEWS

Mechanisms and clinical significance of early recurrences of atrial arrhythmias after catheter ablation for atrial fibrillation

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Abstract

Early recurrence of atrial arrhythmias (ERAA) after ablation is common and strongly predicts late recurrences and ablation failure. However, since arrhythmia may eventually resolve in up to half of patients with ERAA, guidelines do not recommend immediate reintervention for ERAA episodes occurring during a 3-mo post-ablation blanking period. Certain clinical demographic, electrophysiologic, procedural, and ERAA-related characteristics may predict a higher likelihood of long-term ablation failure. In this review, we aim to discuss potential mechanisms of ERAA, and to summarize the clinical significance, prognostic implications, and treatment options for ERAA.

Key words: Atrial fibrillation; Recurrence; Catheter ablation; Pulmonary vein isolation

Core tip: There have been several studies examining the predictors of early recurrences of atrial arrhythmias (ERAA) during the blanking period after atrial fibrillation (AF) ablation and the predictive value of such early recurrences on late recurrences. In this review, we summarize the mechanisms and predictors, clinical significance, prognostic implications, and treatment options of ERAA after AF ablation.

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INTRODUCTION

Catheter ablation is an effective treatment option for patients with symptomatic atrial fibrillation (AF). The

cornerstone of AF ablation involves pulmonary vein isolation (PVI). Early recurrences of atrial arrhythmia (ERAA) are frequent in the post-ablation period, and may occur as either AF or organized atrial tachycardia (OAT), and in some instances may resolve over time without requiring repeat intervention. These early recurrences are thought to be related to post-ablation inflammation, edema, and healing. As such, the consensus guideline statements have recommended employing a 3-mo "blanking period" after AF ablation during which AF or OAT recurrences should not be considered as ablation failure[1]. In this review, we will define and discuss the implications of ERAA, as well as summarize the literature with regards to methods to prevent and treat ERAA.

BLANKING PERIODS AND EARLY RECURRENCES

The use of a blanking period has been employed under the assumption that not all ERAA episodes results in late recurrences. The 2012 HRS/EHRA/ECAS expert consensus statement recommends the use of a 3-mo blanking period after ablation, during which time ERAA episodes not be classified as treatment failure. However, the authors of the guideline statement do state that the use of a shorter blanking period (< 3 mo) is acceptable as long as it is pre-specified and described in the study methods[1]. In line with the consensus statement, most operators tend to avoid repeat ablation for ERAA occurring within the blanking period unless patients are extremely symptomatic with recurrences which are refractory to antiarrhythmic drugs (AADs) and repeated cardioversions.

Variable blanking periods have been utilized across published studies, ranging anywhere from 72 h up to 3 mo post-ablation[2]. While the HRS/EHRA/ECAS consensus statement selected 3 mo as the blanking period of choice, the optimal blanking period to maximize the sensitivity and specificity of prognostic implication of ERAA- and therefore the optimal cutoff interval during which early re-ablation should be avoided, remains poorly studied.

DETECTION OF ERAA IN THE BLANKING PERIOD

Methods of monitoring used to detect ERAA episodes have varied between studies. There is a wide range of intensiveness with regards to duration and strategy of monitoring, and detection of ERAA is dependent on type of monitoring post-ablation. The least intensive monitoring strategies involve symptom-driven 12-lead electrocardiogram, and 24-h or 48-h Holter monitoring ordered only when patients endorse symptoms of palpitations or notice an abnormal pulse. More intensive strategies which studies have utilized include handheld symptom-driven rhythm monitor applications, 30-d transtelephonic monitors, and auto-triggered external and implantable subcutaneous loop recorders. Landmark trials in patients with cryptogenic stroke have demonstrated that more intensive rhythm monitoring for longer durations using transtelephonic monitoring devices (*i.e.*, CardioNet, Malvern, PA; LifeWatch, Rosemont, IL; Medicomp, Melbourne, FL) or implantable cardiac monitors (*i.e.*, Reveal XT and Reveal LINQ; Medtronic, Minneapolis, MN) may increase the likelihood of detecting asymptomatic AF[3,4]. However, since most operators tend to avoid early reablation for paroxysmal recurrences of asymptomatic ERAA during the blanking period, the optimal method of post-ablation monitoring (or whether any monitoring is necessary at all, for that matter) remains controversial.

FREQUENCY OF ERAA

In a pooled analysis by Andrade *et al*[2], the incidence of ERAA after radiofrequency catheter ablation across multiple studies utilizing a 3-mo blanking period ranged from 16%-67% with a mean pooled estimate of approximately 38%. The incidence of ERAA is highest immediately post-ablation and tends to decrease over time throughout the blanking period[5,6]. Rates of ERAA appear to be similar after ablation with radiofrequency or cryoablation, although there may be differences in the predictive value of inflammatory responses on the incidence of ERAA post-ablation between techniques.

For example, in the multicenter Sustained Treatment of Paroxysmal Atrial Fibrillation trial, which randomized patients with paroxysmal AF to medical therapy *vs* PVI with cryoballoon ablation, 51% of patients treated with cryoablation experienced ERAA within the first 3 months post-ablation, and those with ERAA (*vs* without ERAA) were significantly more likely to experience late recurrence (55.6% *vs* 12.7%; $P < 0.001$)[7].

Ciconte *et al*[8] studied 100 patients with persistent AF treated with PVI using second-generation cryoballoon *vs* radiofrequency ablation and found that the rates of both ERAA (51.9% *vs* 48.1%; $P = 1.0$) and late recurrence (47.6% *vs* 52%; $P = 0.84$) were similar between ablation technologies. Among all patients, ERAA in their study predicted late recurrence with a hazard ratio of 6.31 (CI: 3.37-11.83, $P < 0.01$).

In a nonrandomized fashion, Miyazaki *et al*[9] prospectively examined 82 consecutive patients with paroxysmal AF treated with PVI using either radiofrequency ablation *vs* cryoablation with the second generation cryoballoon. While the peak hs-CRP level was similar between ablation techniques, the level of hs-CRP 2 days post-ablation predicted development of ERAA in those treated with radiofrequency (HR = 1.7; 95%CI: 1.01-2.87; $P = 0.048$) but not cryoablation, suggesting that degree of inflammatory marker response may have a stronger predictive value for ERAA after radiofrequency compared with cryoablation.

Table 1 Characteristics which are predictive of the development of early recurrences of atrial arrhythmias after atrial fibrillation ablation

Clinical characteristics
Older age[5]
Male gender[7]
Hypertension[5]
Structural heart disease[10,20]
Longer AF duration[5]
Nonparoxysmal AF type[5]
CHA2DS2-VASc, R2CHADS2 scores[11]
Imaging characteristics
Left atrial size/volume[5]
Right atrial size/volume[12]
Left ventricular size/volume[13]
Left ventricular systolic dysfunction[14]
Left ventricular diastolic dysfunction[15]
Left atrial epicardial adipose tissue[16]
Ablation procedural characteristics
Incomplete PVI[13,20]
AF inducibility[21]
Multiple AF foci[10]
LA free wall AF foci[10]
Lack of AF termination during procedure[22]
Lack of SVC isolation[5]
Inflammatory markers
Higher body temperature post-ablation[17]
C-reactive protein[17]
Homocysteine[18]
Increased LA roof thickness with delayed enhancement MRI 24 h post-ablation[19]

Table modified from Andrade *et al*[2]. AF: Atrial fibrillation; PVI: Pulmonary vein isolation; MRI: Magnetic resonance imaging.

PREDICTORS OF ERAA

Prior studies have identified clinical and demographic characteristics, arrhythmia characteristics, electrocardiographic and echocardiographic characteristics, and AF ablation procedural and post-procedural characteristics which are predict the development of ERAA after ablation, several of which we have listed in Table 1[2,5,7,10-22].

MECHANISMS AND PATHOPHYSIOLOGY OF ERAA

The incidence and clinical significance of ERAA after surgical MAZE is strikingly similar to that of catheter ablation. Approximately 50%-60% of patients develop in-hospital ERAA after MAZE, and those with ERAA have a higher rate of late recurrence (30%) *vs* those whose hospital course is not complicated by ERAA (5%-10%)[23,24].

The mechanism of ERAA after catheter ablation probably differs from that of late recurrences, and is likely dependent on the initial ablation strategy. In patients with paroxysmal AF treated with limited ablation strategies focused primarily on achieving PVI, we have found that late recurrence is usually due to chronic reconnection of previously isolated PVs. In patients with persistent AF treated with empiric linear ablation or those who undergo more extensive substrate-based ablation, gaps in lines may predispose to the development of late macroreentrant OATs. ERAA within the first 7 d post ablation occurs in the setting of an intensely inflammatory milieu. As such, it is difficult to differentiate in the early post-ablation period whether ERAA results from transient post-ablation inflammation (which is likely to resolve without the need for repeat ablation) *vs* chronic PV reconnection. Furthermore, using a rigorous trigger induction protocol, we have identified that non-PV triggers of AF may exist in 11% of patients presenting for AF ablation[25]. Thus the persistence of non-PV triggers due to inadequate identification and elimination of non-PV triggers during the initial ablation procedure can allow for both ERAA and late recurrences to occur.

Lim *et al*[26] measured the blood concentration of several inflammatory markers (hs-CRP, Troponin T, CK-MB, fibrinogen, and D-dimer) before ablation, and serially at different time periods (1, 2, 3, 7 d, and 1 mo) after ablation and correlated the degree of inflammatory marker elevation with AF recurrence documented at different time points post-ablation. They found that the degree of elevation of hs-CRP, troponin-T, and fibrinogen predicted ERAA within 3 d post-ablation, but not at 3 or 6 mo.

Das *et al*[27] examined the association between timing of ERAA with the likelihood of PV reconnection at repeat electrophysiology study in 40 patients with nonparoxysmal AF treated with PVI. After the index ablation procedure, all 40 patients were brought back for electrophysiology study regardless of whether they had recurrence post-ablation. The operator was blinded to the presence and timing of ERAA, and all PVs were assessed for reconnection using a circular mapping catheter. All identified sites of reconnection were related to reisolate PVs, regardless of the presence or absence of ERAA. In total, 17 (42%) of the patients had ERAA within the first 2 months after ablation, preceding the repeat electrophysiology study. The authors found that ERAA occurring within the second month was strongly associated with PV reconnection, and also strongly predicted "extensive reconnection" of $\geqslant$ 2 PVs. Contrarily, ERAA limited to the first month post-ablation had no association with PV reconnection. The results of the study suggested that ERAA within the first month was more likely to be related to transient factors such as inflammation, temporary autonomic imbalances, and the time-course of lesion formation, while ERAA occurring after the first month was more likely to represent ablation failure and PV reconnection[28].

Ablation strategies

The initial ablation strategy may affect the prognostic implications of ERAA. With approaches which involve more extensive substrate-based ablation, ERAA is more likely to be related to edema and inflammation, and accordingly may be more likely to resolve with

time. Meanwhile, ERAA in patients treated with less extensive ablation approaches mainly (*i.e.*, targeting PV and non-PV triggers, for example), may be more likely to represent PV reconnection or inadequate trigger elimination. Since these triggers are unlikely to resolve spontaneously without intervention over time, eventual reablation may be necessary for these patients to achieve freedom from AF.

Post-hoc analysis of data from the Substrate and Trigger Ablation for Reduction of Atrial Fibrillation trial [which compared PVI alone, ablation of complex fractional atrial electrograms (CFAE) alone, and PVI plus CFAE] showed that patients treated with PVI alone who experienced ERAA (*vs* those without ERAA) had significantly higher rates of late recurrence[29]. Interestingly, the predictive value of ERAA on late recurrence was not as strong among those treated with CFAE or PVI plus CFAE. This suggests that substrate-based approaches involving extensive ablation may cause higher incidence of AF related to acute reversible changes post-ablation.

We at our institution employ a strategy aimed at elimination of PV and non-PV triggers. In our experience, patients with recurrent AF after ablation who present for repeat ablation nearly always have PV reconnection and/or non-PV triggers[30]. Non-PV triggers which were not targeted during the initial ablation may manifest as PACs during the ERAA period post-ablation, and may predict late AF recurrence. Gang *et al*[31] examined 7-d Holter monitors in 124 patients six months post-PVI (3 mo after the blanking period had ended) and found that frequent premature atrial complexes (PACs) strongly predicted late AF recurrence. Patients who developed late recurrence had a median of 248 PACs per day compared *vs* those without late recurrence (77 PACs per day). Based on receiver operating characteristic curve analysis, the authors calculated that the presence of $\geqslant$ 142 PACs/d predicted late AF recurrence with a hazard ratio of 2.84 (95%CI: 1.26-6.43; P = 0.01). While their study did not examine the predictive value of PACs during the ERAA blanking period, one could hypothesize that atrial ectopy originating from PV and non-PV foci manifesting as PACs during the blanking period might represented inadequately targeted triggers or partial PV reconnection.

ERAA CHARACTERISTICS WHICH PREDICT LATE RECURRENCE

The occurrence of ERAA after ablation is well known to be a strong independent predictor of late recurrence and long-term ablation failure. In the pooled analysis of several studies by Andrade *et al*[2], there was a 53.7% late recurrence rate among patients with ERAA compared *vs* only 6.9% in patients without ERAA. Several studies have examined whether certain types of ERAA (AF *vs* OAT or atrial flutter) are more predictive of late ablation success. While some authors have suggested success rates after repeat ablation in patients who recur as OAT (*vs* AF) after their initial ablation attempt, it remains unclear whether OAT in the ERAA period is more or less predictive of late ablation failure[32].

Nalliah *et al*[33] examined 119 consecutive patients with paroxysmal or persistent AF who underwent ablation with PVI and additional ablation (50% underwent mitral isthmus linear ablation, and 18% had additional CFAE ablation) to determine the impact of AF and OAT occurring within the blanking period. Patients were not closely monitored for asymptomatic AF during the blanking period, but ERAA as AF was detected in 28% and OAT in 25% within the 3 mo blanking period. Overall, early AF predicted late AF (HR = 3.53; 95%CI: 1.72-7.29; P = 0.001) and early OAT predicted late OAT (HR = 5.62; 95%CI: 2.88-10.95; P < 0.0001). Interestingly, early AF did not predict late OAT, and early OAT did not predict late AF. The authors also found that AF and OAT occurring in the third month of the blanking period had different predictive values for late recurrence: AF in the third month predicted late AF, although OAT in the third month did not predict late OAT.

We do not routinely do empiric linear ablation at our institution, and the majority of patients experiencing ERAA after ablation have AF only (71%; *vs* 5% with early OAT only and 24% with both early AF/OAT)[28]. In our experience, we have found no differences in the likelihood to develop late recurrences based on ERAA type (AF *vs* OAT) (P = 0.92). Since we employ a limited ablation strategy limited to antral PVI and targeting of non-PV triggers, it is possible that in patients treated with more extensive substrate-based ablation approaches involving linear or CFAE ablation, the presence of ERAA as OAT may suggest the presence of gaps in the ablation lines or incomplete CFAE ablation, resulting in late OAT, frequently necessitating repeat ablation.

The predictive value of ERAA appears to be dependent on both frequency and timing of ERAA within the blanking period. We have shown that in patients treated with a limited ablation strategy focused on PVI and elimination of non-PV triggers, the predictive value of ERAA episodes during the first 6 weeks post-ablation is quite variable based on these factors[28]. In our study, we divided the 6-wk blanking period into three separate intervals (Early: weeks 1-2; Intermediate: weeks 3-4; and Late: weeks 5-6), and found that patients with ERAA in a single interval (OR = 3.2, 95%CI: 1.7-5.8 *vs* no ERAA) are significantly less likely to have late recurrence within 1 year *vs* those with ERAA spanning over multiple intervals (OR = 14.6, 95%CI: 7.3-29.6).

Mugnai *et al*[34] have shown similar prognosis of late ERAA within the blanking period after ablation for paroxysmal AF using second-generation cryoballoon ablation instead of radiofrequency energy. In their study of 331 consecutive patients treated with cryoballoon ablation, all patients with ERAA occurring in the second half of the 3-mo blanking period experienced subse-

quent recurrences after the blanking period- suggesting that ERAA occurring later within the blanking period are more predictive of ablation failure[34].

Willems *et al*[35] recently reported the results of a predefined secondary analysis of the prospective, randomized Adenosine Following Pulmonary Vein Isolation to Target Dormant Conduction Elimination trial where the authors analyzed the significance of ERAA at different times throughout the 3-mo blanking period in predicting late recurrences. They divided ERAA which occurred during month 1, 2, and 3 of the blanking period and found that the 1-year ablation success rate was significantly higher among patients without ERAA (77.2% 1-year freedom from AF), while success rates decreased as ERAA occurred later within the blanking period: 62.6% ERAA in month 1, 36.4% in month 2, and 7.8% in month 3 ($P < 0.0001$), with HR = 1.84 for month 1, 4.45 for month 2, 9.64 for month 3. The authors identified a blanking period of 50 d to yield the greatest discriminatory potential by reviewer operating characteristic analysis, and given the dismal (> 90%) late recurrence rates among patients with ERAA during month 3, the results of this study question whether the 3-mo blanking period should be revised.

PREVENTION OF ERAA

AADs

A number of studies have demonstrated that the use of AADs after ablation reduces the incidence of ERAA and reduces hospitalizations and cardioversions during the blanking period. However, meta-analyses have shown that long-term ablation success remains unaffected by early AAD use[36-38]. This would suggest that AADs might mask the early indicators of failed ablation, which may be allowed to manifest only once AADs are withdrawn. While this may indeed decrease hospitalization rates and healthcare expenditure, it may also simply be delaying the recognition of ablation failure.

The Antiarrhythmics After Ablation of Atrial Fibrillation (5A Study) Randomized 110 patients with PAF to AAD (propafenone, flecainide, sotalol, or dofetilide) *vs* no AAD after AF ablation[39]. Those in the AAD group were less likely to have sustained AF recurrence (> 24 h), AF-related hospital admission, cardioversion, AAD adjustment or drug intolerance (19% *vs* 42%; $P = 0.005$ for primary composite endpoint) six-week post ablation.

The Efficacy of Antiarrhythmic Drugs Short-Term Use After Catheter Ablation for Atrial fibrillation trial was a multicenter prospective randomized controlled trial which compared the use of AADs for 90 d post ablation *vs* control in patients after catheter ablation for paroxysmal AF[40]. The authors aimed to examine whether prevention of ERAA with AADs would promote LA remodeling and therefore improve long-term ablation success. They enrolled 2038 patients (1016 randomized to AADs, 1022 control) and the primary endpoint was AF recurrence (lasting > 30), need for repeat ablation, hospitalization, or use of class Ⅰ or Ⅲ AAD at 1 year. They found that although those in the AAD group were more likely to be free from AF during the 90-d treatment period (59% *vs* 52%; HR = 0.84, 95%CI: 0.73-0.96; $P = 0.01$), there was no difference in any of the primary outcome measures at 1 year post-ablation.

The recurrence of arrhythmia following short-term oral AMIOdarone after CATheter ablation for atrial fibrillation trial was a two-center double-blind, randomized placebo-controlled trial which randomized 212 patients with paroxysmal or persistent AF treated with AF ablation to 8 wk of oral amiodarone *vs* placebo following catheter ablation[41]. The authors aimed to determine whether temporary amiodarone use post-ablation would decrease both early and late recurrences. Patients in the amiodarone group had significantly lower rates of ERAA within the blanking period (34% *vs* 53%; $P = 0.006$) but there was no difference in rates of late recurrence at 6 mo between groups (39% *vs* 48%; $P = 0.18$). Additionally, AF-related hospitalization (RR = 0.43, 95%CI: 0.23-0.77, $P = 0.006$) and the need for cardioversion (RR = 0.36, 95%CI: 0.20-0.62, $P = 0.0004$) within the blanking period was significantly reduced in those treated with short-term amiodarone-driven mainly by those with persistent AF, as demonstrated in a subgroup analysis.

Anti-inflammatory agents: Corticosteroids and colchicine

The pro-inflammatory milieu in the immediate post-ablation period is thought to contribute to the development of ERAA, thus many investigators have examined the utility of anti-inflammatory agents to prevent inflammation-induced ERAA. The two major pharmacologic anti-inflammatory agents which have been studied include corticosteroids and colchicine.

Studies examining the use of steroids post-ablation to reduce ERAA have produced conflicting results. Koyama *et al*[42] randomized 125 patients with PAF to steroids (2 mg/kg IV hydrocortisone given immediately post-procedure, followed by 0.5 mg/kg per day oral prednisone for 3 d) *vs* placebo and found that patients randomized to treatment with corticosteroids were less likely to have ERAA within 3 d (7% *vs* 31%), but had similar rates of ERAA between days 4-30. Kim *et al*[43] randomized 138 patients to treatment with steroids *vs* control after ablation. Patients randomized to steroids in their study were treated with intravenous methylprednisolone (0.5 mg/kg per dose) for 2 d followed by 12 mg of oral methylprednisolone for 4 d. Those treated with steroids had a lower rate of ERAA in the 3 mo blanking period (23.4% *vs* 48.6%, $P = 0.003$) but there was no difference in late recurrence rate up to 24 mo ($P = 0.918$). In their multivariate model, the use of steroids was independently associated with lower rate of ERAA (OR = 0.45; 95%CI: 0.25-0.83, $P = 0.01$).

The anti-inflammatory agent colchicine has also been tested as an antiarrhythmic agent to prevent ERAA after AF ablation. In a double-blind fashion, Deftereos

et al[44] randomized 80 patients with paroxysmal AF to colchicine (0.5 mg twice daily for 3 mo) *vs* placebo after AF ablation (antral PVI and left atrial isthmus ablation). Patients randomized to the colchicine arm had lower levels of inflammatory markers post-ablation (C-reactive protein and IL-6) compared with placebo, and were less likely to experience ERAA within the 3-mo blanking period (16% *vs* 33.5%; OR = 0.38; 95%CI: 0.18-0.8) *vs* placebo. In a larger subsequent study, Deftereos *et al*[45] found that patients randomized to colchicine for 3 mo post-ablation had a significantly lower single-procedure late AF recurrence rate after a median follow-up duration 15 mo (31.1% *vs* 49.5%; OR = 0.46; 95%CI: 0.26-0.81). Colchicine is a relatively benign medication (with its major side-effect being gastrointestinal upset), and the results of these preliminary studies are certainly promising. However, future, larger prospective studies are required to confirm the benefit of colchicine after ablation before it can be widely accepted.

TREATMENT OF ERAA

Timing of cardioversion

In patients experiencing ERAA after AF ablation, early cardioversion might improve long-term ablation success. Restoration of sinus rhythm may prevent AF-induced progression of adverse LA remodeling, thus facilitating maintenance of sinus rhythm. Chilukuri *et al*[46] examined timing to cardioversion (before *vs* after the 3-mo blanking period) in patients with nonparoxysmal AF treated with ablation and reported an extremely low (16%) rate of long-term ablation success in patients treated with early cardioversion for persistent AF/OAT during the blanking period, although the rate of long-term freedom from AF was even more dismal (8%) among those who underwent late cardioversion after the blanking period. Baman *et al*[47] examined the effect of the timing of cardioversion after ERAA in 93 patients treated with antral PVI for AF. They found that time to cardioversion was inversely correlated with long-term freedom from AF off AAD: Those who were cardioverted within 30 d (*vs* those cardioverted after 30 d) of ERAA were more likely to remain in sinus rhythm over the remainder of the study duration (OR = 22.5, 95%CI: 4.87-103.88, $P < 0.0001$). Additionally, time between ERAA and cardioversion was the only independent predictor of sinus rhythm maintenance in their multivariate model.

At our institution we aim to restore sinus rhythm as soon as possible in patients with ERAA since we believe that maintenance of sinus rhythm allows for favorable structural, electrical, and mechanical remodeling of the atria and may maximize the likelihood of achieving long-term ablation success. However, it remains to be determined whether the benefits of this approach are similar between paroxysmal and non-paroxysmal types of AF.

Early reablation

The optimal timing for repeat ablation in patients with ERAA remains unknown. As discussed throughout this review, a number of factors including arrhythmia characteristics, patient characteristics, ablation procedural characteristics, and recurrence characteristics play a role in predicting long-term ablation success. The goal is to identify patients in whom ERAA is not just due to transient post-ablation factors, and in whom ablation early in the recurrence course may be more likely to result in long-term ablation success. In a study by Lellouche *et al*[14], of 302 patients with persistent and paroxysmal AF, they reported their experience of 302 patients with persistent and paroxysmal AF, 151 patients had ERAA, 61 of whom were treated with very early reablation (within 1 mo of the index ablation). They found that patients who underwent early reablation had a significantly lower rate of late recurrences (51% *vs* 91%; $P < 0.0001$), although they required more total procedures over the entire follow-up period (2.5 ± 0.7 *vs* 2.2 ± 0.6; $P = 0.02$). Additionally, Andrade *et al*[7] found that patients with ERAA after cryoablation in the STOP AF trial who underwent early reablation during the blanking period were significantly less likely to have late recurrences out to 1 year follow-up (33% *vs* 56% late recurrence rate; HR = 0.04, 95%CI: 0.01-0.32; $P = 0.002$). While their results suggest that early reablation within the blanking period for ERAA after cryoablation improves long-term ablation success, the authors acknowledge that it is possible that reablation may not have been necessary in all patients since it is possible that ERAA may have resolved spontaneously in some.

Recently, Yanagisawa *et al*[48] performed a retrospective analysis examining outcomes after early reablation during the first 3 months post-ablation in 66 patients with ERAA. Compared to 66 propensity-matched controls who did not undergo early reablation, the patients treated with early reablation had a significantly lower rate of late recurrence (64% *vs* 44%; $P = 0.023$), but required more additional procedures (0.4 *vs* 1.2 procedures; $P = 0.001$). Interestingly, the benefit of early reablation for ERAA was limited to those with paroxysmal AF (37% *vs* 66% late recurrence rate for early reablation *vs* no early reablation; $P = 0.008$), while there was no significant benefit to early reablation in those with persistent AF (56% *vs* 60%; $P = 0.77$). Furthermore, 36% of those with ERAA who did not undergo early reablation had no further recurrences in after the 3-mo blanking period.

We have recently shown that in patients with non-paroxysmal AF treated with a limited ablation strategy of antral PVI and targeting of non-PV triggers, patients who recur as paroxysmal (rather than persistent) AF type are more likely to experience long-term ablation success[49]. We believe that patients with persistent or longstanding persistent AF who experience paroxysmal-type ERAA after ablation may represent a subgroup of patients in whom early reablation (even during the blanking period)

can improve long-term ablation success. Transformation of nonparoxysmal AF to paroxysmal AF may represent favorable alteration of the underlying substrate, and we hypothesize that early intervention before AF is allowed to become persistent again (and cause adverse LA electrical and structural remodeling) might result in improved outcomes.

CONCLUSION

Early recurrences of atrial arrhythmia are common in the post-ablation period, and detection of ERAA is dependent on the monitoring strategy. Although ERAA clearly predicts late AF recurrences, some patients with ERAA do not develop late recurrence and thus the guidelines recommend a 3-mo blanking period during which recurrences should not be considered as ablation failure. However, ERAA episodes which occur later within the blanking period (particularly after the first 2 weeks) as well as multiple ERAA occurrences appear to be strongly predictive of late recurrence. Thus, the optimal blanking period during which ERAA events may be benign remains unclear. While pharmacologic agents such as AADs and corticosteroids reduce the incidence of ERAA, they do not improve long-term ablation success. Colchicine is a promising medication which has been shown in isolated studies to decrease both early and late recurrences but larger prospective studies are necessary to validate this effect. Whether reablation should be performed in patients experiencing ERAA remains undetermined. Further studies are necessary to elucidate the optimal timing for reablation based on patient and ERAA characteristics to maximize long-term ablation success.

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