Early Versus Late Atrial Fibrillation Recurrence After Pulsed Field Ablation: Insights From the admIRE Trial

Short Title: PFA in PAF: Early vs Late Recurrence

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Tweet: Early atrial arrhythmia recurrence after pulsed-field ablation of atrial fibrillation is associated with a significant risk of late recurrence. #PFA #Afib

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Data Statement

Johnson & Johnson MedTech has an agreement with the Yale Open Data Access (YODA) Project to serve as the independent review panel for the evaluation of requests for clinical study

reports and patient-level data from investigators and physicians for scientific research that will advance medical knowledge and public health. Requests for access to the study data can be submitted through the YODA Project site at http://yoda.yale.edu.

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STRUCTURED ABSTRACT

Background and Aims: Studies have shown correlations between early recurrence (ER) and late recurrence (LR) of atrial arrhythmia after ablation with thermal technologies. This admIRE trial (NCT05293639) subanalysis aims to analyze ER versus LR in patients with paroxysmal atrial fibrillation (PAF) undergoing pulsed field ablation (PFA).

Methods: Patients with symptomatic paroxysmal atrial fibrillation and ≥1 transtelephonic monitoring transmission during the blanking period were included (n=169). ER was defined as documented recurrence in the blanking period (days 1–90), and LR as recurrence in the evaluation period (days 91–365). Freedom from 12-month recurrence was estimated using Kaplan–Meier method. A Cox proportional-hazards regression model, with ER as the primary factor, and adjusted for age, sex, and body mass index, was used to estimate hazard ratios (HRs) and 95% CI.

Results: ER was observed in 20.1% (31/169) of patients (66.1±7.1 years, 35.5% female, 46.6±48.4-month PAF history). Time to first documented ER was 49 (37–61) days. Occurrence of LR was 16.7% (23/138) in patients without ER, 71.0% (22/31) in those with ER, and 87.0% (20/23) in patients whose ER onset occurred within the first 2 months. Twelve-month freedom from documented recurrence was significantly lower in patients with ER at 29.0% (95% CI,

13.1%–45.0%), versus 82.5% (95% CI, 75.9–89.1%) in those without ER (adjusted HR, 7.9; 95% CI, 4.1–15.1; $P<0.001$).

Conclusion: This admIRE subanalysis demonstrated that PAF patients who experience ER after PFA are at a substantially higher risk for LR. The optimal duration of the blanking period post PFA need further assessments.

Key Words (3–6): early recurrence, late recurrence, atrial fibrillation, ablation, PFA, Varipulse

ABBREVIATIONS

AAD, antiarrhythmic drugs

AF, atrial fibrillation

EAM, electroanatomical mapping

ER, early recurrence

HR, hazard ratio

LR, late recurrence

PAF, paroxysmal atrial fibrillation

PFA, pulsed field ablation

RF, radiofrequency

TTM, transtelephonic monitoring

INTRODUCTION

Early recurrence (ER) post catheter ablation may occur and impact the overall success and prognosis of the procedure. Understanding the implications of ER and its relationship to late recurrence (LR) is crucial for improving patient outcomes and guiding clinical decision making.

Studies have shown correlations between ER and LR after catheter ablation with thermal technologies.[1-6] Recurrence during the first three months postablation has been shown to be a predictor of long-term recurrence using radiofrequency (RF) technologies in patients with atrial fibrillation (AF).[4,5] Similar results were observed in cryoballoon studies,[2,3] leading to the early suggestions of shortening the blanking period from the previously defined three months. The CIRCA-DOSE trial demonstrated that ER taking place three weeks postablation was a predictor for LR.[1] There is scarce evidence on the correlation between ER and LR in patients being treated with pulsed field ablation (PFA). Thus far, only the PULSED AF trial and an additional case series of patients with AF undergoing PFA showed a positive correlation between ER and LR in subanalyses.[7,8]

The present subanalysis therefore aims to analyze early versus late atrial arrhythmia recurrence in patients with paroxysmal atrial fibrillation (PAF) undergoing PFA using a variable loop PFA catheter.

METHODS

Study Design and Ablation Procedure

The admIRE trial (NCT05293639) was a multicenter, prospective, nonrandomized, single-arm interventional study to assess the safety and effectiveness of a variable loop PFA catheter (Varipulse Catheter, Biosense Webster Inc., part of Johnson & Johnson MedTech, Irvine, CA, USA) with an integrated electroanatomical mapping system (CARTO Software,

Biosense Webster Inc., part of Johnson & Johnson MedTech, Irvine, CA, USA). Full details of the admIRE trial study design and ablation procedure have been previously reported.[9] The study catheter was utilized for pulmonary vein isolation. If additional left atrial arrhythmias were identified during the index procedure, ablation outside of the pulmonary veins was allowed using the study catheter for segmental application delivery (≥6 electrodes or circumferential applications with 10 electrodes). In some cases with typical right atrial flutter, cavotricuspid isthmus (CTI) linear ablation using a commercially approved radiofrequency ablation catheter was authorized. The institutional ethics review boards at each study center approved the study, and all enrolled patients provided informed consent prior to moving forward with study procedures.

Patient Follow-Up and Monitoring

Monitoring for arrhythmia recurrence was previously described in detail.[8] Transtelephonic monitoring (TTM; KardiaMobile 6L, AliveCor, Mountain View, CA, USA) was performed weekly from months 1 to 5, monthly from months 6 to 12, and for symptomatic events. TTM transmissions for months 1 and 2 were optional per the study protocol. A 12-lead electrocardiogram was completed at months 3, 6, and 12, and 24-hour Holter monitoring was also performed at months 6 and 12. All recordings were reviewed by an independent core laboratory.

Definitions and Study Outcomes

ER was defined as documented recurrence in the blanking period (days 1–90), while LR was defined as documented recurrence in the evaluation period (days 91–365). The primary endpoint for this subanalysis was LR in patients who exhibited ER in comparison to those who did not.

Statistical Analysis

Baseline and procedural characteristics were presented descriptively as median and interquartile range (IQR) or count and percentage, and compared by means of Wilcoxon rank-sum test or Fisher's exact test, as appropriate. Freedom from recurrence at 12 months was estimated using the Kaplan–Meier method. A Cox proportional-hazards regression model, with ER as the primary factor and LR as the dependent variable, adjusted for age, sex, body mass index, AF duration, cardiomyopathy, and LA diameter was used to estimate hazard ratio (HR) and 95% CI. Statistical analyses were performed using SAS 9.4 or SAS Studio 3.8 (SAS Institute, Inc, Cary, NC).

RESULTS

Patient Characteristics With or Without Early Recurrence

A total of 169 patients from 26 sites with symptomatic paroxysmal atrial fibrillation and ≥1 TTM transmission during the blanking period was included in this analysis. The median age was 65 (IQR 58-68) years, with a median time since diagnosis of 24 (IQR 12-70) months, and 35.5% were female. ER was observed in 18.3% (31/169) of patients whose characteristics were comparable to those of patients without ER (n=138), with the exception of age (68.0 [62.0–72.0] vs. 64.0 [57.0–68.0] years) and CHA_2DS_2–VASc (2.0 [1.0–3.0] vs. 1.0 [1.0 – 3.0], **Table 1**. The median (IQR) time to first documented ER was 49 (37–61) days.

Procedural Characteristics

The procedure time, mapping time, and fluoroscopy times between patients with vs. without ER were comparable: 96.0 (86.0 – 120.0) vs. 98.5 (72.0 – 121.0), 6.0 (4.0 – 11.0) vs. 7.0 (5.0 – 10.0), and 6.1 (1.1 – 14.1) vs. 6.6 (0.0 – 13.4), respectively (**Table 2**). ICE was used in

about 94% of cases in each cohort. The number of valid PFA applications per patient were also similar with 65.0 (58.0 – 73.0) in the ER group and 70.0 (60.0 – 85.0) in the non-ER group.

A total of 1 (3.2%) of patients in the ER group and 14 (10.1%) in the non-ER group received additional posterior wall segmental ablation. In addition, 5 (16.1%) and 23 (16.7%) received additional cavotricuspid isthmus ablation (**Table 2).**

Early Versus Late Recurrence Correlation

The occurrence of LR was 16.7% (23/138) in patients without ER. LR occurrence was 71.0% (22/31) in those with ER and 87.0% (20/23) in patients whose ER onset occurred within the first 2 months (**Figure 1**). The 12-month freedom from documented atrial tachyarrhythmia recurrence was found to be significantly lower in patients with ER at 29.0% (95% CI, 13.1%–45.0%), compared to 82.5% (95% CI, 75.9–89.1%) in those without ER (adjusted HR, 7.9; 95% CI, 4.1–15.1; $P < 0.001$, **Figure 2**).

Further analysis to understand the negative predictive values (NPV) and positive predictive values (PPV) were performed (**Table 3**). The PPV at 2-month ER was 87.0 (73.2–100.0) compared to 3-month ER with a PPV of 71.0 (55.0–87.0). In addition, the NPV for 2-month ER was 82.5 (76.3–88.7) versus 3-month ER at 83.0 (76.6–89.3).

AAD Utilization

About 5.3% (9/169) of patients took a higher dose or new Class I/III antiarrhythmic drugs (AAD) during the blanking period (2 higher than the previously failed dose and 7 on new AAD). A total of five ER episodes across five patients were treated with AADs (4 with a new AAD and 1 with a higher dose of a currently taken AAD). Five patients were taking oral anticoagulants

starting on Day 1, unrelated to ER. Over the course of the 12-month follow-up period, 15.7% patients were on Class I/III AADs during months 1-3, 8.7% during months 3-6, and 6.5% during months 6-12, regardless of ER.

Safety

Procedural complication rates, defined as adverse events on the date of the index procedures, between with vs. without ER were 16.1% (5/31) and 6.5% (9/138), respectively. All five of the procedural complication events in the ER group were procedure-related, while five our of the nine without ER were procedure-related. The primary adverse event rates between the two groups were 6.5% (2/31) in the ER group and 1.5% (2/138) in the LR group.

DISCUSSION

The findings of this admIRE trial subanalysis evaluated the incidence and timing of ER in patients with PAF following PVI with PFA and its effect on long-term success, as indicated by freedom from LR over the course of 12 months. We have demonstrated the significance of ER as a predictor of reduced long-term effectiveness.

Larger studies analyzing the correlation between ER and LR in patients with paroxysmal atrial fibrillation (PAF) and persistent AF are needed to fully understand the potential to reduce, and potentially eliminate, the blanking period post-PFA. Awareness of this relationship holds promise in improving patient quality of care.

In this subanalysis of the admIRE study, which included 31 patients with ER, the occurrence of LR was substantially lower in patients without ER (16.7%) than in those with ER (71%) or ER onset within the first 2 months (87%). Twelve-month freedom from documented atrial tachyarrhythmia recurrence was significantly higher in patients without ER (29.0%) than in

those with ER (84.0%; $P < 0.001$). Class I/III AAD use was relatively low (<6%) during the blanking period. In a concordance analysis, there was a high level of agreement between 6- and 12-month freedom from atrial arrhythmia recurrence, regardless of the duration of blanking period.

Similar results to those shown in the current study were observed in a previous secondary analysis of the PULSED AF study, which evaluated the safety and efficacy of a PFA system (PulseSelect Pulsed Field Ablation System; Medtronic, Minneapolis, MN) for treatment of PAF and persistent AF.[7] That secondary analysis, which used similar definitions for ER (recurrence within 90 days postablation) and LR (recurrence between 90 days and 12 months postablation), included 154 patients with PAF and 140 patients with persistent AF, 27% and 32% of whom, respectively, had ER.[7] Overall, the occurrence of LR was lower in patients with no ER (24%) than in those with ER (67%), and this difference was even more pronounced in the subgroup with PAF (no ER, 20%; ER, 71%).[7] The incidence of LR was higher in patients with their last ER episode during 61-90 days postablation (83% overall; 79% for PAF) than in those with their last episode within 1-30 days (47% overall; 67% for PAF) or 31-60 days (42% overall; 56% for PAF).[7]

Also, Mohanty et al. analyzed 337 patients undergoing PFA for AF. Early recurrences were recorded in 15.7% patients.[8] At 1 year follow-up, all patients with recurrence in the second and third months experienced late recurrence. Therefore, the authors concluded that early recurrence in the second or third month after the PFA procedure was associated with a high risk of late recurrence. Thus, the authors suggested that the blanking period could be redefined as little as 1 month after PFA.

Similar analyses have been performed in patients undergoing RF or cryoballoon ablation for AF.[1,3,4] In an analysis including 207 consecutive patients with persistent AF, in which ER was defined as recurrence within the first 30 days postablation, ER occurred in 69.1% of patients.[4] LR, which was defined as recurrence >30 days postablation, occurred significantly more frequently in patients with ER (92.3%) than in those without ER (43.8%; $P < 0.001$).[4] In a registry study of 2,636 patients with PAF or persistent AF undergoing cryoballoon ablation, in which ER was defined as recurrence within 90 days postablation and LR was recurrence >90 days postablation, 1-year freedom from LR was significantly lower in patients with ER (42.6%) than in those without ER (85.5%).[3] Among patients with ER, 1-year freedom from LR was 44.1% for patients with ER within 30 days postablation, 32.4% for ER between 30 to 60 days postablation, and 39.0% for ER between 60 and 90 days postablation ($P = 0.051$).[3] Similar results were shown in the CIRCA-DOSE trial comparing RF ablation with cryoballoon ablation in 346 patients with PAF, in which 61% of patients had ER (defined as recurrence within 90 days postablation).[1] A significantly higher proportion of patients with ER than without ER experienced LR ($P < 0.001$), and later ER episodes (during the third month after blanking) were associated with a higher likelihood of LR than ER episodes in the first or second month.[1]

The analyses of timing of ER and occurrence of LR in the PULSED AF secondary analysis in patients undergoing PFA[7] and similar analyses in patients undergoing RF or cryoballoon ablation[1,3,4] indicate that ER within the third month postablation may be considered LR and have led to the recommendation to shorten the blanking period postablation. A more recent subanalysis using RF in patients with persistent atrial fibrillation also discovered substantially increased long-term arrhythmia recurrence in patients with recurrence during the blanking period compared to those without.[10] The corresponding editorial comments on growing

evidence to shorten the blanking period to two months.[11] Since then, the 2024 European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS/SOLAECE) guidelines recommend a reduced 2-month blanking period[12] compared with the 3-month blanking period recommended in the 2017 HRS/EHRA/European Cardiac Arrhythmia Society/APHRS/SOLAECE guidelines.[13] The 25 years of progress in atrial fibrillation review emphasizes the potential for further improvements in AF mapping and technologies to propel these clinical outcomes, such as reduction in AF recurrence, for patients treated with PFA.[14] Whether this new ablation modality can be considered in the same respect as previous technologies, such as radiofrequency and cryoballoon, is still under further analysis. So far, a propensity score matching study found similar long-term efficacy across the three modalities.[15] Additional therapies, including high power, short duration, have also been considered and have shown comparable recurrence rates.[16] Whether these findings translate into reducing the blanking period is up to further question. In the current study, ER within the 2-month blanking period predicted LR more effectively compared to ER within the protocol-defined 3-months. This higher rate suggests that ER even early on can predict LR, calling into question a 2-month or perhaps a nonexistent blanking period. Nevertheless, results of the current analysis support the association between ER and LR observed in previous studies. This subanalysis may shape future studies to investigate the need for a blanking period using different modalities.

Additional studies on AF ablation treatment have investigated predictors of ER vs. LR, such as C-reactive protein or early pulmonary vein (PV) reconnection.[17,18] While PV reconnection found about 30 minutes post-ablation was associated with LR, the C-reactive

protein had no significant relationship to neither ER nor LR. Further investigations into predictors for ER vs. LR are warranted.

Limitations

The admIRE trial did not require TTM during the protocol-defined blanking period (Months 1– 3). Patients who had a transmitted recording were likely symptomatic and/or more compliant to the study protocol. The sample size therefore would have represented a larger proportion of the overall enrolled patient population if remote monitoring was required during the blanking period. The overall low number of ER events prevented us from performing a time-sensitive analysis stratifying the impact of ER during the first month versus recurrences during the second month post-blanking period.

In addition, not all patients received their TTM devices within the first month after the index ablation. This was due to issues surrounding vendor shipping.

CONCLUSION

This admIRE subanalysis demonstrated that symptomatic PAF patients who experience ER after PFA are at a substantially higher risk for LR. These data underscore the importance of early postablation monitoring and may inform future strategies to mitigate ER and improve long-term clinical outcomes. The optimal duration of the blanking period post PFA requires further assessment.

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REFERENCES

1. Steinberg C, Champagne J, Deyell MW, Dubuc M, Leong-Sit P, Calkins H, et al. Prevalence and outcome of early recurrence of atrial tachyarrhythmias in the Cryoballoon vs Irrigated Radiofrequency Catheter Ablation (CIRCA-DOSE) study. *Heart Rhythm*. 2021;18:1463–1470.
2. Xia Y, Liu J, Jia Y, Zhang H, Yu M, Li X, et al. Redefining the blanking period by a long-term follow-up after atrial fibrillation ablation using second-generation cryoballoon. *Int Heart J*. 2020;61:936–943.
3. Park J, Cha MJ, Kwon CH, Cho MS, Nam GB, Oh IY, et al. Long-term clinical impact of early recurrence of atrial tachyarrhythmia after cryoballoon ablation in patients with atrial fibrillation. *J Cardiovasc Electrophysiol*. 2024;35:1614–1623.
4. Popa MA, Kottmaier M, Risse E, Telishevska M, Lengauer S, Wimbauer K, et al. Early arrhythmia recurrence after catheter ablation for persistent atrial fibrillation: is it predictive for late recurrence? *Clin Res Cardiol*. 2022;111:85–95.
5. Farghaly AAA, Ali H, Lupo P, Foresti S, De Ambroggi G, Atta S, et al. Early versus late radiofrequency catheter ablation in atrial fibrillation: timing matters. *J Clin Med*. 2024;13:4643.

6. Vaishnav AS, Levine E, Coleman KM, Beldner SJ, Chinitz JS, Bhasin K, et al. Early recurrence of atrial fibrillation after pulmonary vein isolation: a comparative analysis between cryogenic and contact force radiofrequency ablation. *J Interv Card Electrophysiol*. 2020;57:67–75.

7. Boersma LVA, Natale A, Haines D, DeLurgio D, Sood N, Marchlinski F, et al. Prevalence, timing, and impact of early recurrence of atrial tachyarrhythmias after pulsed field ablation: a secondary analysis of the PULSED AF trial. *Heart Rhythm*. 2024. https://doi.org/10.1016/j.hrthm.2024.06.036.

8. Mohanty S, Torlapati PG, Casella M, Della Rocca DG, Schiavone M, Doty B, et al. Redefining the blanking period after pulsed-field ablation in patients with atrial fibrillation. *Heart Rhythm*. Published online August 6, 2024. doi:10.1016/j.hrthm.2024.08.011

9. Reddy VY, Calkins H, Mansour M, Wazni O, Di Biase L, Bahu M, et al. Pulsed field ablation to treat paroxysmal atrial fibrillation: safety and effectiveness in the AdmIRE pivotal trial. *Circulation*. 2024;150:1174–1186.

10. Noujaim C, Lim C, Mekhael M, Feng H, Chouman N, Younes H, et al. Identifying the prognostic significance of early arrhythmia recurrence during the blanking period and the optimal blanking period duration: insights from the DECAAF II study. *Europace*. 2023;25(6):euad173.

11. Mohanty S, Mansour M, Natale A. Identifying the prognostic significance of early arrhythmia recurrence during the blanking period: a pursuit to rediscover the past. *Europace*. 2023;25(9):euad229.

12. Tzeis S, Gerstenfeld EP, Kalman J, et al. 2024 European Heart Rhythm Association/Heart Rhythm Society/Asia Pacific Heart Rhythm Society/Latin American Heart Rhythm Society expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Europace*. 2024;26:euae043.
13. Boersma L, Andrade JG, Betts T, Duytschaever M, Pürerfellner H, Santoro F, et al. Progress in atrial fibrillation ablation during 25 years of Europace journal. *Europace*. 2023;25(9):euad244.
14. Calkins H, Hindricks G, Cappato R, Saad EB, Sepehri Shamloo A, Andrade JG, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Europace*. 2018;20:e1–e160.
15. Della Rocca DG, Marcon L, Magnocavallo M, Menè R, Pannone L, Mohanty S, et al. Pulsed electric field, cryoballoon, and radiofrequency for paroxysmal atrial fibrillation ablation: a propensity score-matched comparison. *Europace*. 2023;26(1):euae016.
16. Reinsch N, Füting A, Hartl S, Höwel D, Rausch E, Lin Y, et al. Pulmonary vein isolation using pulsed field ablation vs. high-power short-duration radiofrequency ablation in paroxysmal atrial fibrillation: efficacy, safety, and long-term follow-up (PRIORI study). *Europace*. 2024;26(7):euae194.
17. Lellouche N, Sacher F, Wright M, Nault I, Brottier J, Knecht S, et al. Usefulness of C-reactive protein in predicting early and late recurrences after atrial fibrillation ablation. *Europace*. 2009;11(5):662-664.
18. Efremidis M, Letsas K, Giannopoulos G, Lioni L, Vlachos K, Asvestas D, et al. Early pulmonary vein reconnection as a predictor of left atrial ablation outcomes for paroxysmal atrial fibrillation. *Europace*. 2015;17(5):741-746.

FIGURE LEGENDS

Figure 1. Proportion of patients with LR (postblanking period).[a] Proportions of patients with LR among patients with no ER, ER, and ER within 2 months. [a]ER: 3-month (days 0-90) recurrence. LR: 3-12 month (days 91-365) recurrence. ER, early recurrence; LR, late recurrence.

Figure 2. Freedom from documented recurrence in the evaluation period (Days 91–365). Freedom from recurrence at 12 months estimated using the Kaplan–Meier method for patients with and without ER. [a]ER: 3-month (days 0-90) recurrence. ER, early recurrence; N, no; Y, yes.

Table 1. Baseline Characteristics

Characteristics[a]	ER[b] (n=31)	No ER (n=138)	p-value
Age, years	68.0 (62.0 – 72.0)	64.0 (57.0 – 68.0)	0.001
Female	11 (35.5)	49 (35.5)	>0.999
Body mass index	28.0 (24.9 – 33.7)	27.8 (24.3 – 30.8)	0.343
LVEF, %	61.0 (57.0 – 65.0)	60.0 (55.0 – 65.0)	0.375
Left atrial diameter, mm	39.0 (36.0 – 44.0)	38.0 (35.0 – 43.0)	0.217
CHA_2DS_2–VASc	2.0 (1.0 – 3.0)	1.0 (1.0 – 3.0)	0.027
PAF History, months	[illegible] (12.0 – 72.0)	24.6 (12.0 – 67.0)	0.940
Myocardial infarction	3 (9.7)	3 (2.2)	0.076
Hypertension	21 (67.7)	72 (52.2)	0.161
Type II diabetes	8 (25.8)	13 (9.4)	0.029
Coronary disease	9 (29.0)	28 (20.3)	0.337
Obstructive sleep apnea	9 (29.0)	39 (28.3)	>0.999

Thromboembolic events	3 (9.7)	4 (2.9)	0.116
Congestive heart failure	1 (3.2)	5 (3.6)	>0.999
NYHA Class I	0 (0.0)	1 (0.7)	>0.999
NYHA Class II	1 (3.2)	4 (2.9)	
Number of failed AADs	1.0 (1.0 – 1.0)	1.0 (1.0 – 1.0)	0.664
Class I/III AAD	1.0 (1.0 – 1.0)	1.0 (1.0 – 1.0)	0.368

[a]Data are presented as median (IQR) or n (%).

[b]ER: 3-month (days 0-90) recurrence.

ER, early recurrence; PAF, paroxysmal atrial fibrillation.

Table 2. Procedural Characteristics

Characteristics[a]	ER (n=31)	No ER (n=138)	p-value
Procedure time, min	96.0 (86.0 – 120.0)	98.5 (72.0 – 121.0)	0.419
Procedure time for PVI, min	93.0 (86.0 – 112.0)	82.0 (64.0 – 114.0)	0.201
Total mapping time, min	6.0 (4.0 – 11.0)	7.0 (5.0 – 10.0)	0.673
Transpired PFA time, min	31.9 (27.5 – 43.9)	31.9 (25.7 – 41.2)	0.468
Fluoroscopy time, min	6.1 (1.1 – 14.1)	6.6 (0.0 – 13.4)	0.865
Cases performed without fluoroscopy	6 (19.4)	35 (25.4)	0.644
Cases in which ICE was used	29 (93.6)	129 (93.5)	<0.999
Cases with only the study catheter for mapping	1 (3.2)	13 (9.4)	0.470
Number of valid PFA applications per patient	65.0 (58.0 – 73.0)	70.0 (60.0 – 85.0)	0.182
Received additional posterior wall segmental ablation	1 (3.2)	14 (10.1)	0.310
Received additional CTI ablation	5 (16.1)	23 (16.7)	>0.999

[a]Data are presented as median (IQR) or n (%).

ER, early recurrence; ICE, intracardiac echocardiography; PFA, pulsed field ablation; PVI, pulmonary vein isolation.

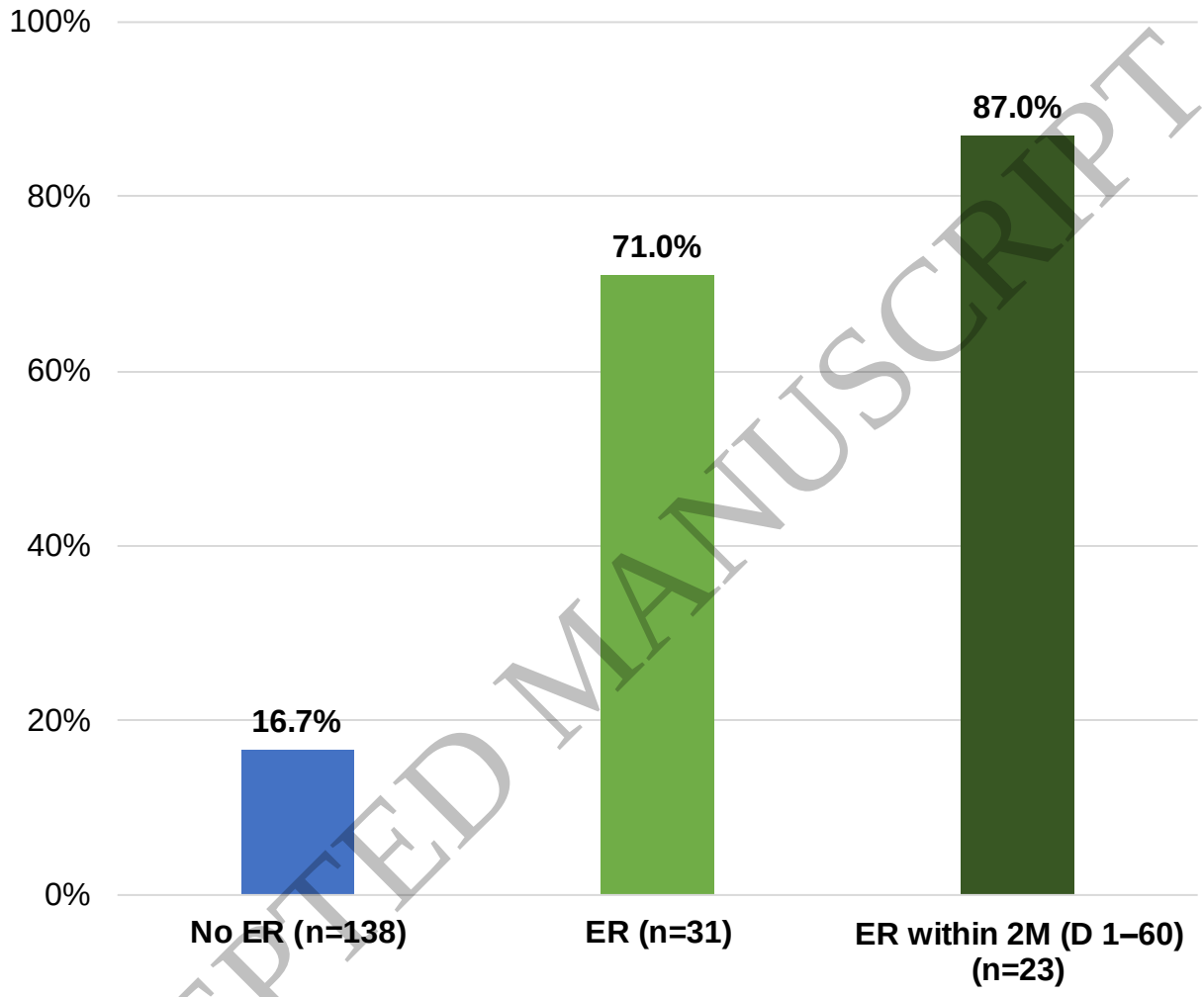
Table 3. PPV and NPV

Statistic	Estimates[a]	
	2M ER	3M ER
Sensitivity	44.4 (29.9–59.0)	48.9 (34.3–63.5)
Specificity	97.5 (94.8–100.0)	92.6 (87.9–97.2)
PPV	87.0 (73.2–100.0)	71.0 (55.0–87.0)
NPV	82.5 (76.3–88.7)	83.0 (76.6–89.3)

[a]Data are presented as percent estimate (95% CI).

CI, confidence interval; ER, early recurrence; M, month; NPV, negative predictive value; PPV, positive predictive value.

Figure 1. Proportion of patients with LR (postblanking period).[a] Proportions of patients with LR among patients with no ER, ER, and ER within 2 months.

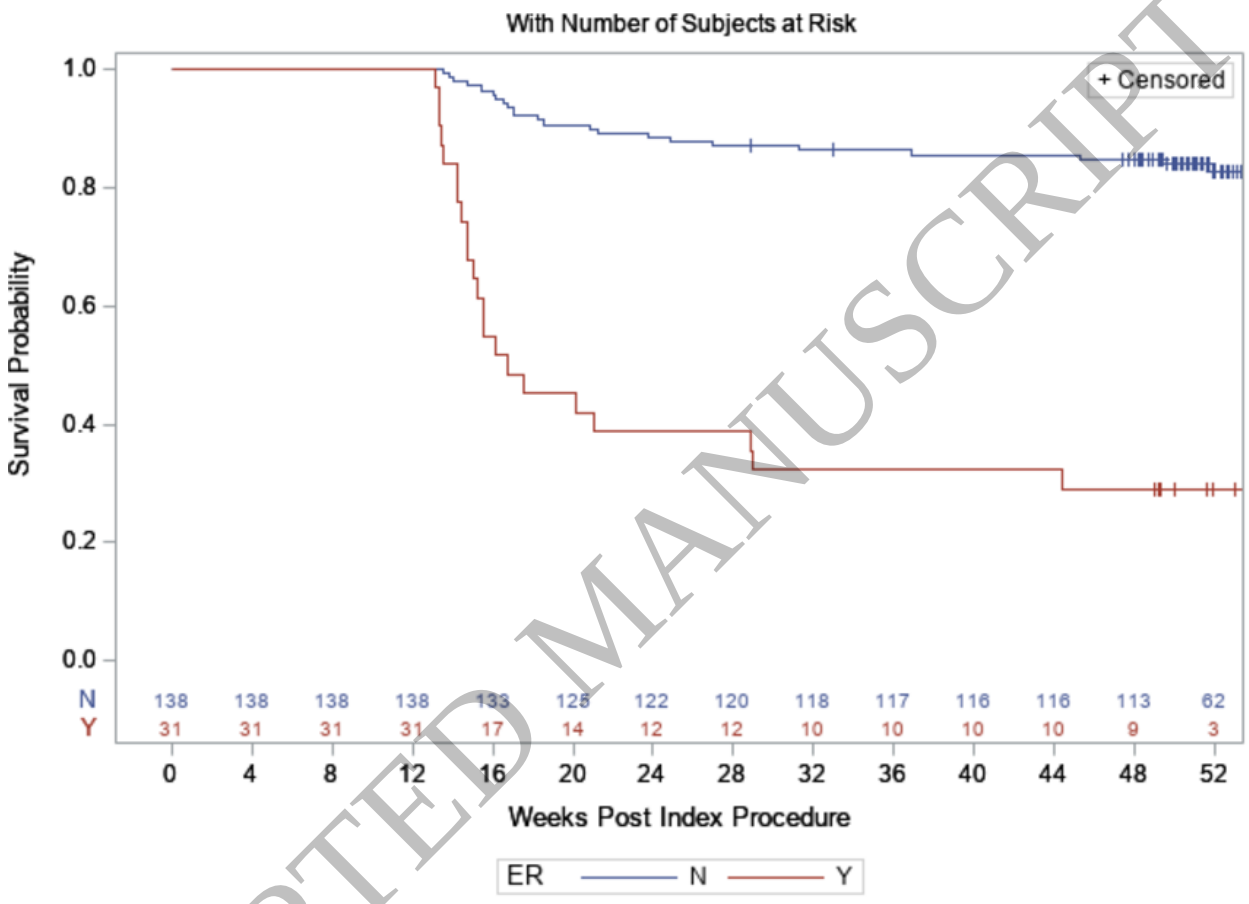


[a]ER: 3-month (days 0-90) recurrence. LR: 3-12 month (days 91-365) recurrence.

ER, early recurrence; LR, late recurrence.

Figure 2. Freedom from documented recurrence in the evaluation period (Days 91–365).

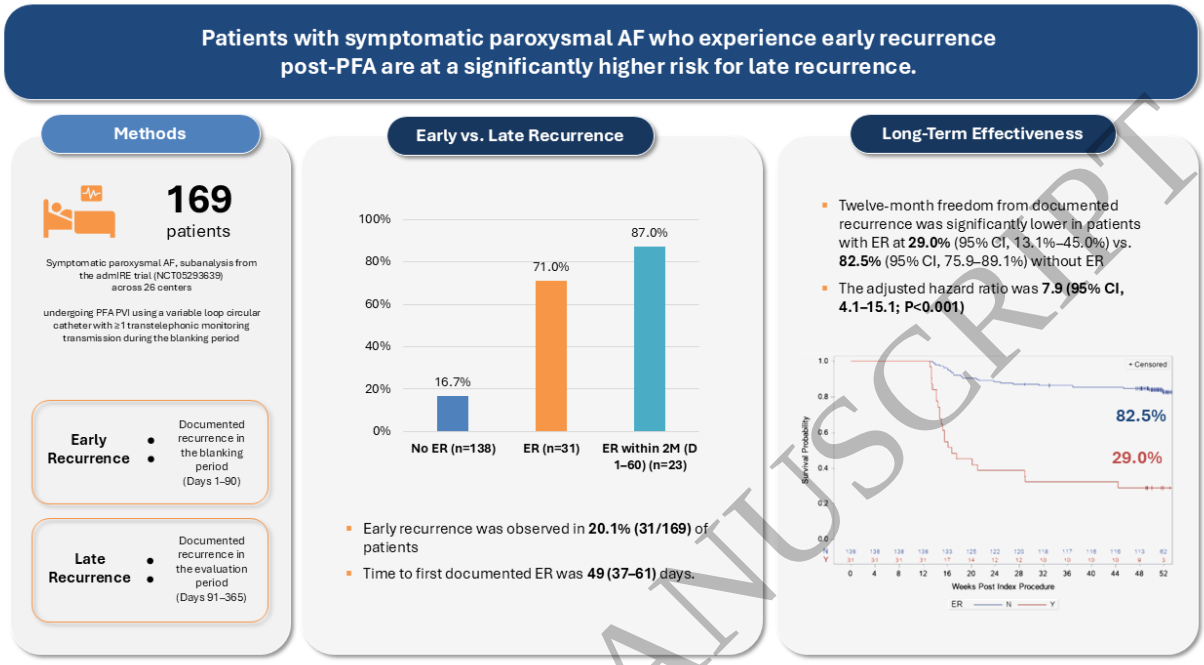
Freedom from recurrence at 12 months estimated using the Kaplan–Meier method for patients with and without ER.



[a]ER: 3-month (days 0-90) recurrence.

ER, early recurrence; N, no; Y, yes.

Graphic Abstract.



AF, atrial fibrillation; CI, confidence interval; D, day; ER, early recurrence; M, month; PAF, paroxysmal atrial fibrillation; PFA, pulsed field ablation; PVI, pulmonary vein isolation.