Circulation: Arrhythmia and Electrophysiology

ORIGINAL ARTICLE

Relationship Between Time-to-First Atrial Tachyarrhythmia Recurrence and Atrial Fibrillation Burden: Implications for Trial Design

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BACKGROUND: Atrial tachyarrhythmia recurrence remains the primary end point of clinical trials evaluating therapeutic pharmacological and nonpharmacological interventions for atrial fibrillation (AF). We sought to examine the relationship between the timing of first atrial tachyarrhythmia recurrence and subsequent AF burden.

METHODS: We performed a patient-level analysis of 2 multicenter prospective parallel-group, single-blinded randomized clinical trials that used continuous rhythm monitoring after rhythm intervention. Patients with paroxysmal AF were stratified based on the month where the first recurrence of atrial tachyarrhythmia was observed, after a 2-month blanking period. AF burden was calculated as the time spent in AF at 1 year after first recurrence and over 3 years of follow-up.

RESULTS: A total of 56.5% of patients experienced a first recurrence of atrial tachyarrhythmia within the third month post treatment initiation, with 79.5% of all recurrences detected by month 6 and 90.2% detected by month 9. The median postrecurrence AF burden was significantly greater in those with first recurrence in month 3 (1.04% [interquartile range, 0.23–5.05]) when compared with those patients with first recurrence between months 4 to 12 (0.13% [interquartile range, 0.04–0.63]; $P<0.0001$ versus month 3) and those with first recurrence after month 12 (0.05% [interquartile range, 0.01–0.20]; $P<0.0001$ versus month 3).

CONCLUSIONS: Atrial tachyarrhythmia recurrence after rhythm control intervention for paroxysmal AF is not uniform, with earlier recurrences being associated with higher long-term AF burden. These findings suggest that the timing of arrhythmia recurrence is of critical importance, with later recurrences being of progressively lesser clinical significance.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: atrial fibrillation ■ atrial flutter ■ catheter ablation ■ pulmonary veins ■ tachycardia

For nearly 20 years, the primary end point of clinical trials evaluating pharmacological and nonpharmacological interventions for atrial fibrillation (AF) has been the time-to-first occurrence of any atrial tachyarrhythmia (AF, atrial flutter, or atrial tachycardia) at 1 year of follow-up.[1–4] However, this end point suffers from several limitations, mainly the use of a binary threshold implies that all durations of arrhythmia are weighted equally in terms of their impact on patient outcomes.[5–7] This oversimplification inadequately reflects clinically relevant outcomes, neglects the complexity of the patient experience, and fails to consider meaningful differences in arrhythmia recurrence based on the index time to recurrence.

Given these limitations, there has been a recent push to reconsider arrhythmia recurrence end points. AF burden, or the proportion of the observed time that a patient is in AF, is a quantifiable outcome that has been associated

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Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/CIRCEP.125.013971.
For Sources of Funding and Disclosures, see page XXX.

Circulation: Arrhythmia and Electrophysiology is available at www.ahajournals.org/journal/circep

WHAT IS KNOWN?

- Atrial tachyarrhythmia recurrence remains the primary end point of clinical trials for atrial fibrillation (AF) but suffers from several limitations, including an assumption that all recurrences of arrhythmia are equally important.
- AF burden is a quantifiable outcome associated with quality of life, AF-related healthcare utilization but necessitates the use of continuous cardiac rhythm monitoring, which is invasive, costly, and impractical for widespread use.

WHAT THE STUDY ADDS

- Atrial tachyarrhythmia recurrence after rhythm control intervention for paroxysmal AF is not uniform, and the timing of arrhythmia recurrence is of critical importance, with most treatment failures occurring in the first month of active arrhythmia monitoring post blanking, and these earlier recurrences are associated with higher long-term AF burden.
- When the primary outcome of a clinical trial is to detect clinically relevant burdens of AF, it may be reasonable to decrease the trial follow-up duration from 12 to 6 months of follow-up, resulting in substantial operational savings and facilitating earlier dissemination of results.

Nonstandard Abbreviations and Acronyms

AF	atrial fibrillation
ICM	implantable cardiac monitor
IQR	interquartile range

with changes in quality of life and AF-related healthcare utilization (emergency room visit, all-cause hospitalization, cardioversion, and repeat ablation).[6,8–20] However, accurate assessment of AF burden necessitates the use of continuous cardiac rhythm monitoring (eg, with implantable cardiac monitors [ICMs]),[5,21,22] which is invasive and costly, rendering it impractical for widespread use.

The goal of the current study was to leverage continuous monitoring data from 2 large multicenter randomized controlled trials of rhythm control interventions for paroxysmal AF. This large cohort of patients with long-term continuous rhythm enabled us to examine the relationship between the timing of first atrial tachyarrhythmia recurrence and subsequent AF burden, with the goal of informing optimal end points and follow-up duration for trials of AF interventions.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

We performed a patient-level analysis of 2 multicenter prospective parallel-group, single-blinded randomized clinical trials: CIRCA-DOSE (Cryoballoon Versus Irrigated Radiofrequency Catheter Ablation; URL: https://www.clinicaltrials.gov; Unique identifier: NCT01913522) and the EARLY AF (Early Aggressive Invasive Intervention for Atrial Fibrillation; NCT02825979).[23–26] The CIRCA-DOSE trial was an investigator-initiated, multicenter, parallel-group, single-blinded randomized clinical trial, with blinded end point adjudication conducted at 8 centers in Canada.[23,26] The EARLY AF trial was an investigator-initiated, multicenter, open-label, randomized trial with blinded end point adjudication at 18 centers in Canada.[24,25] Both studies were approved by the institutional ethics and review board of each participating center, with academic steering committees being responsible for the study design, conduct, and reporting. All subjects provided informed consent.

Details of the 2 trial protocols have been reported previously.[27,28] In brief, these 2 trials included patients aged >18 years with symptomatic paroxysmal AF that was either treatment naive (EARLY AF) or refractory to at least 1 class I or class III antiarrhythmic drug (CIRCA-DOSE). Patients were randomized to initial antiarrhythmic drugs or first-line cryoballoon pulmonary vein isolation (EARLY AF), or to 1 of 3 different pulmonary vein isolation strategies (CIRCA-DOSE). In both trials, all patients underwent insertion of an ICM before treatment initiation. The ICM was used for determination of arrhythmia recurrence, as well as to accurately quantify AF episode duration and AF burden, the latter being defined as the percentage of time in AF. Patients were followed for up to 3 years after treatment initiation (ablation therapy or antiarrhythmic drug initiation) with clinical visits, a 12-lead ECG, and supplementary 24-hour ambulatory ECG monitoring at 3, 6, and 12 months, then every 6 months thereafter.

Atrial Tachyarrhythmia

The complete rhythm history was reconstructed for each participant using daily assessment of arrhythmia burden from the implanted ICM. The time and duration of every atrial tachycardia/AF episode were tabulated on a per-patient basis.

The primary outcome of both trials was time to first symptomatic or asymptomatic atrial tachyarrhythmia (AF, atrial flutter, or atrial tachycardia) documented by 12-lead ECG, 24-hour ambulatory ECG monitor, or ICM between days 91 and 365 post ablation. In both trials the atrial tachyarrhythmia events meeting standardized arrhythmia detection settings were stored for adjudication by an independent, blinded clinical end point committee.

For both trials, an initial blanking period was used. For the ablation groups, the blanking period was meant to exclude early recurrences of atrial tachyarrhythmia post ablation, as these do not necessarily predict later treatment failure.[29] The blanking period in the antiarrhythmic group allowed for medication optimization. For the purpose of the current analysis, we have adjusted the blanking period from 90 to 60 days as recommended in the 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 AF.[4]

AF burden was defined as the proportion of the total monitored interval that a patient was in AF. The gold-standard AF

Table 1. Patient Characteristics

Factor	CIRCA-DOSE	EARLY-AF	*P* value
N	346	303	
Age, y, mean (SD)	58.7861 (9.96664)	58.604 (11.522)	0.83
Female sex	115 (33.2%)	89 (29.4%)	0.29
BMI, mean (SD)	29.1055 (5.25013)	29.6471 (9.36294)	0.36
Hypertension	120 (34.7%)	112 (37.0%)	0.55
Coronary disease	25 (7.2%)	19 (6.3%)	0.63
Heart failure	6 (1.7%)	28 (9.2%)	<0.001
Stroke	16 (4.6%)	9 (3.0%)	0.27
Sleep apnea	45 (13.0%)	64 (21.1%)	0.006
Diabetes	29 (8.4%)	27 (8.9%)	0.81
Smoker	17 (4.9%)	18 (5.9%)	0.56
CHA_2DS_2-VASc, median (IQR)	1 (0–2)	1 (0–2)	0.82
LA dimension, mean (SD)	39.207 (5.38355)	38.7721 (5.85068)	0.43
LA vol, mean (SD)	35.2238 (15.1877	35.1479 (13.5924)	0.96
LVEF, mean (SD)	59.2133 (6.07656)	60.0214 (6.18616)	0.14

Data are mean±SD, median (IQR), or n (%). The CHA_2DS_2-VASc score is a clinical estimation of the risk of stroke in patients with atrial fibrillation, with scores ranging from 0 to 9, with higher scores indicating a greater risk. AF indicates atrial fibrillation; BMI, body mass index; CIRCA-DOSE, Cryoballoon Versus Irrigated Radiofrequency Catheter Ablation; EARLY AF, Early Aggressive Invasive Intervention for Atrial Fibrillation; IQR, interquartile range; LA, left atrium; and LVEF, left ventricular ejection fraction.

burden was derived from the ICM[30] and calculated as the time in AF divided by the total follow-up time (ie, in the 1 year after first atrial tachyarrhythmia recurrence and at 1 and 3 years from treatment initiation, excluding a 2-month postablation blanking period), on a per-patient basis. Given AF burden of >0.1% has been associated with increased healthcare utilization,[6] we also examined the proportion of patients with AF burden >0.1% based on recurrence month.

Statistical Analysis

Patients were stratified based on the month where the first recurrence of atrial tachyarrhythmia was observed, which was additionally trichotomized into patients with first recurrence in month 3, months 4 to 12, and after month 12, dates chosen based on the consensus document recommendations.[1–4]

Normally distributed continuous variables are presented as mean±SD, and non-normally distributed variables are presented as median (interquartile range [IQR]). Differences in AF burden were assessed using nonparametric Kruskal-Wallis test, with between-group differences evaluated using Dunn multiple comparisons test. Recurrence timing and CIs were evaluated using the Kaplan-Meier method. Analyses were performed using MatLab (MathWorks; Natick, MA), Stata 15 (StataCorp. College Station, TX), and Prism 8 (GraphPad Software; San Diego, CA).

RESULTS

The study population consisted of 649 patients treated with first-line antiarrhythmic drug therapy (149), first-line catheter ablation (154), and catheter ablation after antiarrhythmic drug failure (346) in the EARLY AF and CIRCA-DOSE randomized clinical trials.[23–26] Patient characteristics are presented in Table 1. Patients enrolled in CIRCA-DOSE had lower rates of clinical heart failure and obstructive sleep apnea but were otherwise comparable to the EARLY AF population. Patients were followed for up to 3 years, during which time a total of 614 231 days of arrhythmia monitoring were performed.

Recurrence Timing Over the First Year of Follow-Up

Of the 649 patients included, 336 patients experienced an episode of atrial tachyarrhythmia lasting longer than 30 seconds between 61 and 365 days after treatment initiation. Of these patients, 56.5% (95% CI, 52.9%–60.3%) experienced a first recurrence of atrial tachyarrhythmia within the third month post treatment initiation (ie, the first month of active arrhythmia monitoring after the 2-month blanking period). A further 10.7% (95% CI, 6.9%–14.2%) of patients experienced a first recurrence in month 4, and 6.8% (95% CI, 3.0%–10.5%) in month 5. Thereafter, the recurrence risk was low (≈≤5%; Figure 1). When considering rhythm control treatment, 67.6% (95% CI, 59.0%–76.5%) of those patients receiving first-line antiarrhythmic drug therapy experienced a first recurrence of atrial tachyarrhythmia within the third month posttreatment initiation compared with 51.0% (95% CI, 44.7%–57.0%) undergoing catheter ablation (Figure S1). Patients with recurrence in month 3 were more likely be treated with antiarrhythmic drug therapy and undergo catheter ablation during follow-up (Table 2).

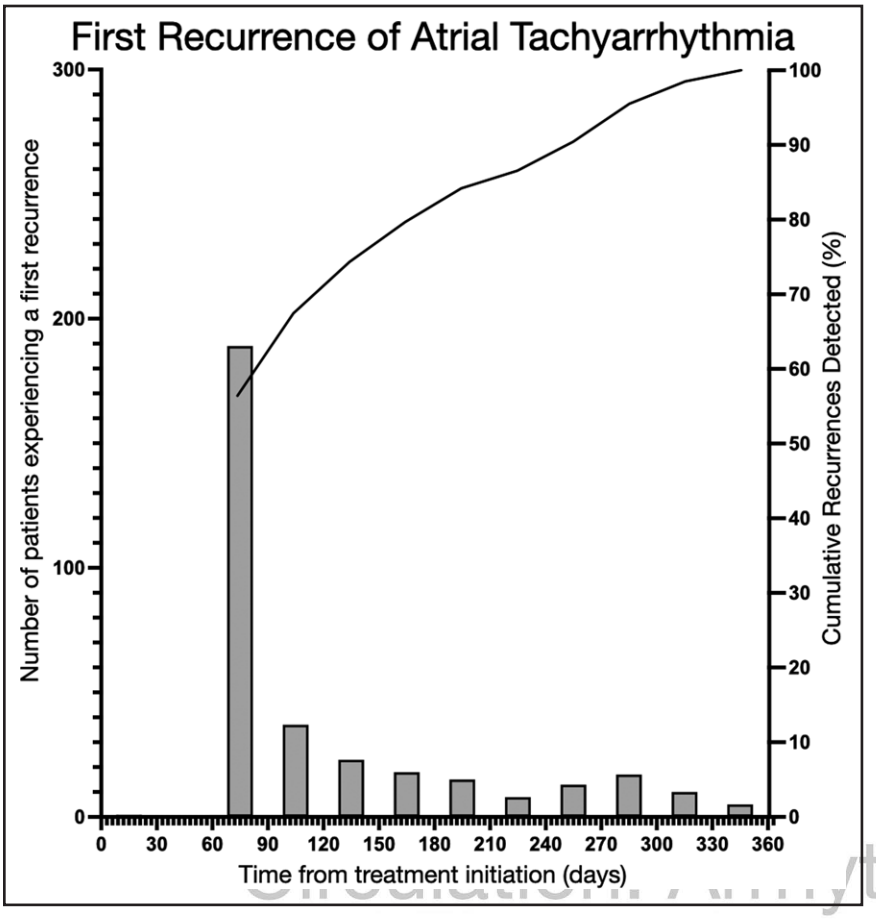

Figure 1. Distribution of first atrial tachyarrhythmia recurrence in the study population, stratified by month after treatment initiation.
Bars indicate the number of patients experiencing a first atrial tachyarrhythmia recurrence, and the solid line indicates the cumulative percentage of patients experiencing atrial tachyarrhythmia recurrence.

AF Burden

Median AF burden was 0.01% (IQR, 0.00–0.41) at 1 year and 0.03% (IQR, 0.00–0.37) at 3 years after treatment initiation for the entire study cohort. In those with documented AF recurrence, the median AF burden was 0.17% (IQR, 0.01–1.22) at 1 year after treatment initiation and 0.19% (IQR, 0.04–0.83) at 3 years after treatment initiation. The median AF burden was 0.25% (IQR, 0.02–1.29) in the first year following the first recurrence of atrial tachyarrhythmia.

Median AF burden in the year after index recurrence (postrecurrence burden, Figure 2) was significantly greater in those with first recurrence in month 3 (1.04% [IQR, 0.23–5.05]) when compared with those patients with first recurrence between months 4 to 12 (0.13% [IQR, 0.04–0.63]; $P<0.0001$ versus month 3), and those with first documented recurrence after month 12 (0.05% [IQR, 0.01–0.20]; $P<0.0001$ versus month 3). There was no difference in AF burden between those with first recurrence between months 4 to 12 and those after month 12 ($P=0.44$).

Similar findings were observed when examining the median AF burden over 3 years of follow-up (Figure S2), which was significantly greater in those with first recurrence in month 3 (0.62% [IQR, 0.17–2.97]) when compared with those patients with first recurrence between months 4 to 12 (0.09% [IQR, 0.03–0.38]; $P<0.0001$ versus month 3), and those with first documented recurrence after month 12 (0.02% [IQR, 0.00–0.09]; $P<0.0001$ versus month 3).

These findings did not differ when stratified by the rhythm controlling treatment received, with those undergoing catheter ablation and those randomized to first-line antiarrhythmic drug therapy both demonstrating significantly higher AF burdens on follow-up when the first recurrence occurred in the third month posttreatment initiation (Figure 3).

Eliminating the postprocedure blanking period (Figure S3) amplified the early arrhythmia detection, with 80.8% of recurrences detected in the first month after treatment initiation. However, the overall AF burden in this group was low (0.37% at 1 year postindex recurrence and 0.21% at 3 years) and did not differ from those of patients with first recurrence detected throughout the remainder of the first year of follow-up. Moreover, 60 patients reclassified as treatment failure through blanking period elimination had no further documented atrial tachyarrhythmia over 3 years of follow-up.

Reducing Follow-Up Duration From 12 to 6 Months

The impact of a shorter follow-up duration is presented in Figure 4. A total follow-up duration of 6 months from

Table 2. Patient Characteristics by Month of First Recurrence

Factor	Month 3	Months 4–12	>12 mo	*P* value
N	190	145	70	
Age, y, mean (SD)	60.9053 (9.53254)	58.4483 (12.1157)	59.8714 (9.02801)	0.10
Sex	64 (33.7%)	50 (34.5%)	24 (34.3%)	0.99
BMI, mean (SD)	29.1325 (6.57653)	29.1118 (6.30037)	29.5345 (6.85036)	0.89
Hypertension	75 (39.5%)	51 (35.2%)	25 (35.7%)	0.69
Coronary disease	14 (7.4%)	12 (8.3%)	4 (5.7%)	0.80
Heart failure	7 (3.7%)	7 (4.8%)	6 (8.6%)	0.27
Stroke	9 (4.7%)	8 (5.5%)	4 (5.7%)	0.93
Sleep apnea	30 (15.8%)	31 (21.4%)	12 (17.1%)	0.41
Diabetes	16 (8.4%)	12 (8.3%)	4 (5.7%)	0.76
Smoker	10 (5.3%)	12 (8.3%)	2 (2.9%)	0.25
CHA_2DS_2-VASc, median (IQR)	1 (0–2)	1 (0–2)	1 (0–2)	0.97
LA dimension, mean (SD)	39.594 (6.33088)	38.4545 (5.74538)	40.4854 (4.46847)	0.13
LA volume, mean (SD)	37.6301 (15.4052)	37.6424 (13.7648)	34.5233 (17.0269)	0.48
LVEF, mean (SD)	58.5481 (5.55933)	59.5911 (6.01605)	60.4508 (6.63515)	0.10
Antiarrhythmic drug use	105 (55.3%)	59 (40.7%)	21 (30.0%)	<0.001
Ablation	112 (58.9%)	58 (40.0%)	8 (11.4%)	<0.001

The CHA_2DS_2-VASc score is a clinical estimation of the risk of stroke in patients with AF, with scores ranging from 0 to 9, with higher scores indicating a greater risk. AF indicates atrial fibrillation; BMI, body mass index; IQR, interquartile range; LA, left atrium; and LVEF, left ventricular ejection fraction.

treatment initiation (eg, 4 months active monitoring plus 2 months blanking) detected 79.5% of all patients with recurrence. Those with a first recurrence by month 6 had a significantly great postrecurrence AF burden (median, 0.58% [IQR, 0.09–2.57]) compared with those with recurrence detected between months 7 and 12 (0.08% [IQR, 0.01–0.47]; $P<0.0001$) and those with first recurrence after month 12 (0.05% [IQR, 0.01–0.21]; $P<0.0001$). Of those patients with first recurrence within 6 months of treatment initiation, 77.9% had a postrecurrence AF burden >0.1%.

DISCUSSION

The current study demonstrates the following key findings. (1) Atrial tachyarrhythmia recurrence after rhythm control intervention is not uniform, with most treatment failures occurring in the first month of active arrhythmia monitoring post blanking, (2) Those patients with first recurrence of atrial tachyarrhythmia in the first month of active arrhythmia monitoring had a significantly higher postrecurrence and total burden of AF compared with those with later recurrences. These findings suggest that

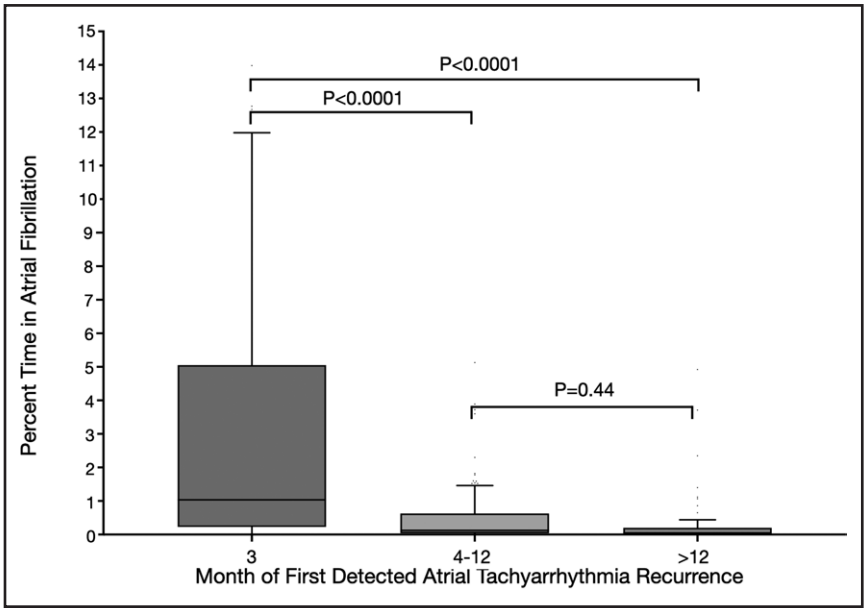

Figure 2. Postrecurrence atrial fibrillation burden, categorized by month of first arrhythmia recurrence.

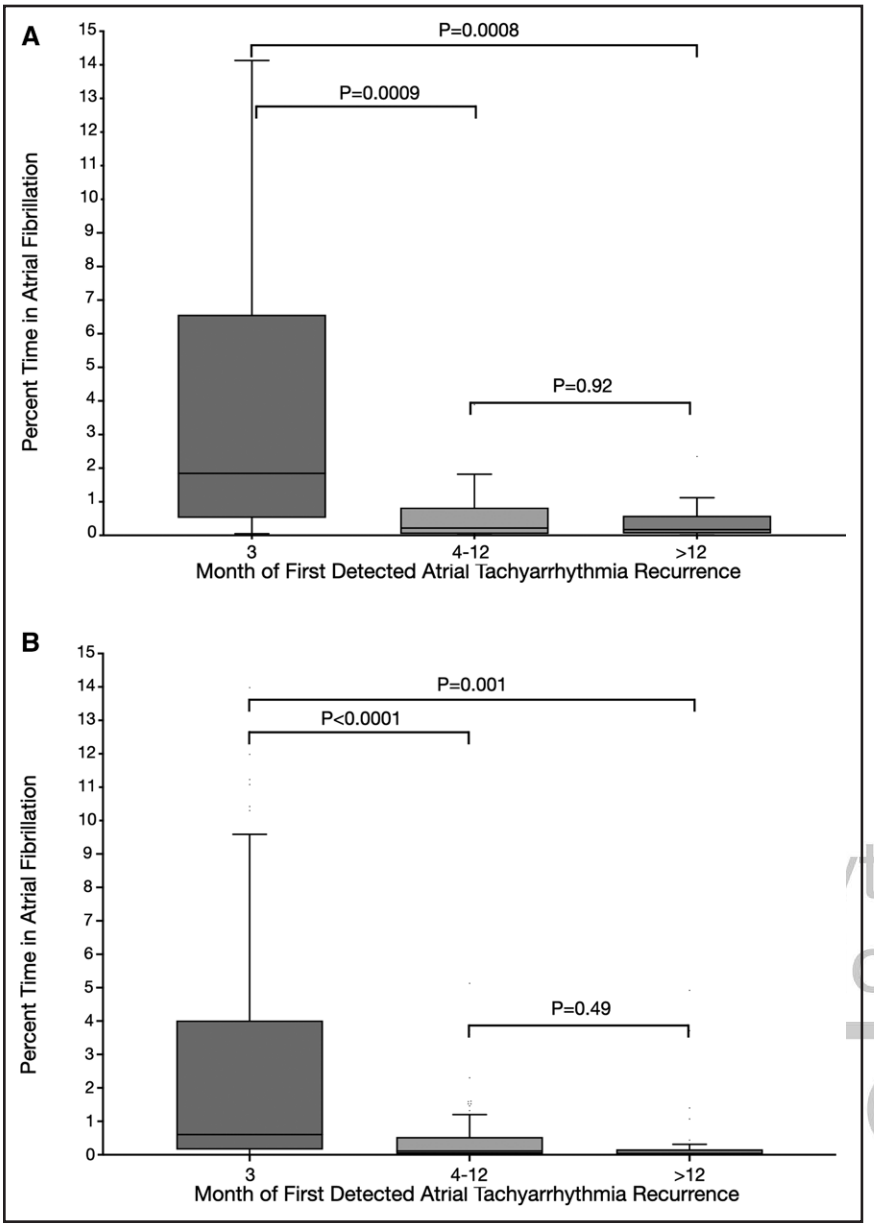

Figure 3. Postrecurrence atrial fibrillation burden, categorized by month of first arrhythmia recurrence. **Top**, Antiarrhythmic drug therapy. **Bottom**, Catheter ablation.

the timing of arrhythmia recurrence is of critical importance, suggesting that earlier recurrences are qualitatively different from later recurrences. Taken together, the current study indicates that not all binary recurrences of atrial tachyarrhythmia are equal and that it would be inappropriate to treat them as such.

Clinical trials evaluating atrial tachyarrhythmia therapies are complex, expensive, and logistically challenging. A key goal of clinical research evaluating the effectiveness of therapeutic interventions for AF is the demonstration of efficacy in preventing arrhythmia recurrence. Based on expert consensus, the recommended minimum duration of follow-up has been set at 12 months, which previously included a 3-month blanking period (ie, 9 months of active arrhythmia monitoring).[1–4] In response to updated evidence, the duration of the blanking period after pulmonary vein isolation has been shortened from 12 weeks to 8 weeks.[4]

We previously demonstrated that most patients with recurrences of atrial tachyarrhythmia in the third month after treatment initiation continued to experience a high burden of atrial tachyarrhythmia, irrespective of subsequent treatment.[31] However, those patients with a first recurrence of atrial tachyarrhythmia after the third month had a relatively low burden of atrial tachydysrhythmia on follow-up.[31] This observation suggested that there was a fundamental difference between those recurrences before and after 3 months of follow-up in terms of the underlying mechanism of recurrence, as well as the clinical relevance of these arrhythmia episodes.

The current study builds on the previous findings by demonstrating in the largest cohort of patients with

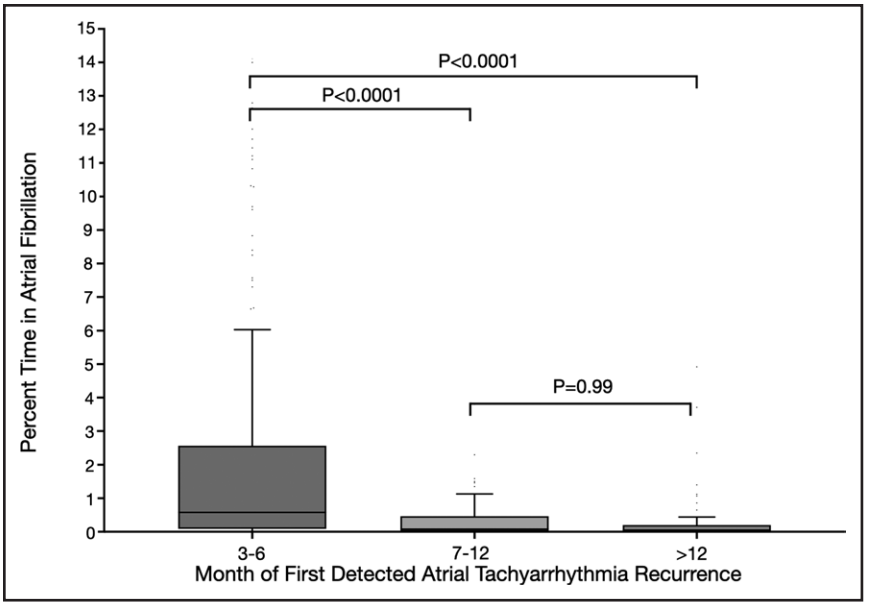

Figure 4. Postrecurrence atrial fibrillation burden, categorized by follow-up interval.

paroxysmal AF undergoing long-term follow-up with continuous rhythm monitoring that not only do the majority of recurrences occur in the first month of active follow-up, but that these recurrences fundamentally differ from those observed later. Specifically, those exhibiting first recurrence in month 3 had the highest AF burden on long-term follow-up (median 0.62% at 3 years). Moreover, significantly more patients experiencing a first recurrence of atrial tachyarrhythmia in month 3 demonstrated a clinically relevant AF burden (>0.1%), a burden threshold associated with impaired quality of life and increased healthcare utilization.[6,14,20] This observation is despite higher rates of antiarrhythmic drug use and ablation in the early recurrence groups, an intervention that would be expected to reduce the subsequent AF burden (Table 2).

As such, when the primary outcome of a clinical trial is to detect clinically relevant burdens of AF, the use of a 12-month follow-up may not be necessary. Approximately 80% of patients will experience a first arrhythmia recurrence within 6 months of treatment initiation (4 months active follow-up plus 2 months procedural blanking), with these patients displaying the greatest AF burden at 1 year post recurrence and at 3 years of follow-up. The subset of patients with first recurrence after month 6 has a lower median AF burden and is less likely to exceed the 0.1% threshold. Given this observation, it may be possible to substantially truncate clinical trial follow-up, resulting in substantial operational savings and facilitating earlier dissemination of results.

Limitations

The participants included in the current analysis had symptomatic paroxysmal AF referred for pharmacological or catheter-based intervention. Although we included participants with treatment naïve AF and antiarrhythmic drug refractory AF, we cannot extrapolate the results to a population with persistent AF. Moreover, as those patients undergoing ablation underwent the procedure using thermal energy (radiofrequency and cryoenergy), we cannot extrapolate the results to alternate energy sources such as pulsed field ablation. In addition, we limited the initial stratification of patients to recurrences observed within the first year of follow-up. The rationale for this restriction was 2-fold. First, this is the duration of follow-up advocated by consensus statements.[1–4] Second, the majority of recurrences occur within the first year after treatment initiation, with only a minority of patients experiencing recurrence after the first year. Third, the inclusion of very late recurrences would limit the ability to evaluate the long-term burden of arrhythmia owing to a prolonged period free of arrhythmia before index recurrence (eg, survivorship bias). By restricting the primary analysis of AF burden to the year after the first atrial tachyarrhythmia recurrence, we have been able to standardize the follow-up interval and effectively eliminate the survivorship bias.

Conclusions

Atrial tachyarrhythmia recurrence after rhythm control intervention for paroxysmal AF is not uniform, with earlier recurrences being qualitatively more important. If the focus of trials is to detect clinically relevant burdens of AF, it may be possible to substantially truncate clinical trial follow-up, resulting in substantial operational savings and facilitating earlier dissemination of results.

ARTICLE INFORMATION

Received April 2, 2025; accepted July 29, 2025.

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Sources of Funding

The current study was unfunded. The CIRCA-DOSE study (Cryoballoon Versus Irrigated Radiofrequency Catheter Ablation) was funded by a peer-reviewed grant from the Heart and Stroke Foundation of Canada (grant number G-13-0003121), with additional financial support from Medtronic and Heart Rhythm Services at the University of British Columbia. The EARLY AF study (Early Aggressive Invasive Intervention for Atrial Fibrillation) was funded by a peer-reviewed grant from the Cardiac Arrhythmia Network of Canada (grant number SRG-15-P15-001), which is a Networks of Centres of Excellence program funded from a joint initiative of the Natural Sciences and Engineering Research Council, the Social Sciences and Humanities Research Council, the Canadian Institutes of Health Research, Industry Canada, and Health Canada. In addition, the trial was supported by unrestricted grants from Medtronic and Baylis Medical, as well as in-kind support from Medtronic (implantable cardiac monitors) and the University of British Columbia. The funding sources had no role in the design of this study and did not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Disclosures

Dr Aguilar discloses honoraria from Biosense-Webster and Abbott. Dr Deyell discloses grant support and consulting fees from Biosense-Webster, honoraria from Boston Scientific, and consulting fees and honoraria from Medtronic and Kardium. Dr Macle discloses honoraria from Biosense-Webster, Boston Scientific, and Abbott. Dr Andrade discloses honoraria from Medtronic, Biosense-Webster, Boston Scientific, and Abbott. The other authors report no conflicts.

Supplemental Material

Figures S1–S3

REFERENCES

1. Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJ, Damiano RJ Jr, Davies DW, Haines DE, Haissaguerre M, et al; Heart Rhythm Society. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation developed in partnership with the European Heart Rhythm Association (EHRA) and the European Cardiac Arrhythmia Society (ECAS); in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), and the Society of Thoracic Surgeons (STS). Endorsed and approved by the governing bodies of the American College of Cardiology, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, and the Heart Rhythm Society. *Europace*. 2007;9:335–379. doi: 10.1093/europace/eum120
2. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ Jr, Davies DW, DiMarco J, et al; Heart Rhythm Society Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society. *Heart Rhythm*. 2012;9:632.e21–696.e21. doi: 10.1016/j.hrthm.2011.12.016
3. Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm*. 2017;14:e275–e444. doi: 10.1016/j.hrthm.2017.05.012
4. Tzeis S, Gerstenfeld EP, Kalman J, Saad EB, Sepehri Shamloo A, Andrade JG, Barbhaiya CR, Baykaner T, Boveda S, Calkins H, 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. doi: 10.1093/europace/euae043
5. Aguilar M, Macle L, Deyell MW, Yao R, Hawkins NM, Khairy P, Andrade JG. Influence of monitoring strategy on assessment of ablation success and postablation atrial fibrillation burden assessment: implications for practice and clinical trial design. *Circulation*. 2022;145:21–30. doi: 10.1161/CIRCULATIONAHA.121.056109
6. Andrade JG, Deyell MW, Macle L, Steinberg JS, Glotzer TV, Hawkins NM, Khairy P, Aguilar M. Healthcare utilization and quality of life for atrial fibrillation burden: the CIRCA-DOSE study. *Eur Heart J*. 2023;44:765–776. doi: 10.1093/eurheartj/ehac692
7. Doehner W, Boriani G, Potpara T, Blomstrom-Lundqvist C, Passman R, Sposato LA, Dobrev D, Freedman B, Van Gelder IC, Glotzer TV, et al. Atrial fibrillation burden in clinical practice, research, and technology development: a clinical consensus statement of the European Society of Cardiology Council on Stroke and the European Heart Rhythm Association. *Europace*. 2025;27:euaf019. doi: 10.1093/europace/euaf019
8. Verma A, Haines DE, Boersma LV, Sood N, Natale A, Marchlinski FE, Calkins H, Sanders P, Packer DL, Kuck KH, et al; PULSED AF Investigators. Influence of monitoring and atrial arrhythmia burden on quality of life and health care utilization in patients undergoing pulsed field ablation: a secondary analysis of the PULSED AF trial. *Heart Rhythm*. 2023;20:1238–1245. doi: 10.1016/j.hrthm.2023.05.018
9. Schwennesen HT, Andrade JG, Wood KA, Piccini JP. Ablation to reduce atrial fibrillation burden and improve outcomes: JACC review topic of the week. *J Am Coll Cardiol*. 2023;82:1039–1050. doi: 10.1016/j.jacc.2023.06.029
10. Turakhia MP, Ziegler PD, Schmitt SK, Chang Y, Fan J, Than CT, Keung EK, Singer DE. Atrial fibrillation burden and short-term risk of stroke: case-crossover analysis of continuously recorded heart rhythm from cardiac electronic implanted devices. *Circ Arrhythm Electrophysiol*. 2015;8:1040–1047. doi: 10.1161/CIRCEP.114.003057
11. Go AS, Reynolds K, Yang J, Gupta N, Lenane J, Sung SH, Harrison TN, Liu TI, Solomon MD. Association of burden of atrial fibrillation with risk of ischemic stroke in adults with paroxysmal atrial fibrillation: the KP-RHYTHM study. *JAMA Cardiol*. 2018;3:601–608. doi: 10.1001/jamacardio.2018.1176
12. Piccini JP, Passman R, Turakhia M, Connolly AT, Nabutovsky Y, Varma N. Atrial fibrillation burden, progression, and the risk of death: a case-crossover analysis in patients with cardiac implantable electronic devices. *Europace*. 2019;21:404–413. doi: 10.1093/europace/euy222
13. Brachmann J, Sohns C, Andresen D, Siebels J, Sehner S, Boersma L, Merkely B, Pokushalov E, Sanders P, Schunkert H, et al. Atrial fibrillation burden and clinical outcomes in heart failure: the CASTLE-AF trial. *JACC Clin Electrophysiol*. 2021;7:594–603. doi: 10.1016/j.jacep.2020.11.021
14. Samuel M, Khairy P, Champagne J, Deyell MW, Macle L, Leong-Sit P, Novak P, Badra-Verdu M, Sapp J, Tardif JC, et al. Association of atrial fibrillation burden with health-related quality of life after atrial fibrillation ablation: substudy of the Cryoballoon vs Contact-Force Atrial Fibrillation Ablation (CIRCA-DOSE) randomized clinical trial. *JAMA Cardiol*. 2021;6:1324–1328. doi: 10.1001/jamacardio.2021.3063
15. Steinberg BA, Li Z, O'Brien EC, Pritchard J, Chew DS, Bunch TJ, Mark DB, Nabutovsky Y, Greiner MA, Piccini JP. Atrial fibrillation burden and heart failure: data from 39,710 individuals with cardiac implanted electronic devices. *Heart Rhythm*. 2021;18:709–716. doi: 10.1016/j.hrthm.2021.01.021
16. Chew DS, Li Z, Steinberg BA, O'Brien E, Pritchard J, Bunch TJ, Mark DB, Patel MR, Nabutovsky Y, Greiner MA, et al. Association between economic and arrhythmic burden of paroxysmal atrial fibrillation in patients with cardiac implanted electronic devices. *Am Heart J*. 2022;244:116–124. doi: 10.1016/j.ahj.2021.11.006
17. Tang SC, Liu YB, Lin LY, Huang HC, Ho LT, Lai LP, Chen WJ, Ho YL, Yu CC. Association between atrial fibrillation burden and cognitive function in patients with atrial fibrillation. *Int J Cardiol*. 2023;377:73–78. doi: 10.1016/j.ijcard.2023.01.007
18. Chew DS, Li Z, Steinberg BA, O'Brien EC, Pritchard J, Bunch TJ, Mark DB, Patel MR, Nabutovsky Y, Greiner MA, et al. Arrhythmic burden and the risk of cardiovascular outcomes in patients with paroxysmal atrial fibrillation

and cardiac implanted electronic devices. *Circ Arrhythm Electrophysiol.* 2022;15:e010304. doi: 10.1161/CIRCEP.121.010304
19. Sciacca V, Sohns C, Crijns H, Marrouche NF, Schramm R, Moersdorf M, Fink T, Bergau L, Hindricks G, Dagres N, et al. Effects of atrial fibrillation ablation on arrhythmia burden and ventricular function in end-stage heart failure: lessons from CASTLE-HTx. *Eur J Heart Fail.* 2025;27:255–263. doi: 10.1002/ejhf.3505
20. Reddy VY, Gerstenfeld EP, Schmidt B, Andrade JG, Nair D, Natale A, Saliba W, Sommer P, Metzner A, Verma A, et al; ADVANTAGE AF Investigators. Pulsed field ablation of persistent atrial fibrillation with continuous ECG monitoring follow-up: ADVANTAGE AF-phase 2. *Circulation.* 2025;152:27–40. doi: 10.1161/circulationaha.125.074485
21. Charitos EI, Stierle U, Ziegler PD, Baldewig M, Robinson DR, Sievers HH, Hanke T. A comprehensive evaluation of rhythm monitoring strategies for the detection of atrial fibrillation recurrence: insights from 647 continuously monitored patients and implications for monitoring after therapeutic interventions. *Circulation.* 2012;126:806–814. doi: 10.1161/CIRCULATIONAHA.112.098079
22. Charitos EI, Ziegler PD, Stierle U, Robinson DR, Graf B, Sievers HH, Hanke T. Atrial fibrillation burden estimates derived from intermittent rhythm monitoring are unreliable estimates of the true atrial fibrillation burden. *Pacing Clin Electrophysiol.* 2014;37:1210–1218. doi: 10.1111/pace.12389
23. Andrade JG, Champagne J, Dubuc M, Deyell MW, Verma A, Macle L, Leong-Sit P, Novak P, Badra-Verdu M, Sapp J, et al; CIRCA-DOSE Study Investigators. Cryoballoon or radiofrequency ablation for atrial fibrillation assessed by continuous monitoring: a randomized clinical trial. *Circulation.* 2019;140:1779–1788. doi: 10.1161/CIRCULATIONAHA.119.042622
24. Andrade JG, Deyell MW, Verma A. Cryoablation as initial therapy for atrial fibrillation. Reply. *N Engl J Med.* 2021;384:e82. doi: 10.1056/NEJMc2103408
25. Andrade JG, Deyell MW, Macle L, Wells GA, Bennett M, Essebag V, Champagne J, Roux JF, Yung D, Skanes A, et al; EARLY-AF Investigators. Progression of atrial fibrillation after cryoablation or drug therapy. *N Engl J Med.* 2023;388:105–116. doi: 10.1056/NEJMoa2212540
26. Andrade JG, Deyell MW, Khairy P, Champagne J, Leong-Sit P, Novak P, Sterns L, Roux JF, Sapp J, Bennett R, et al. Atrial fibrillation progression after cryoablation vs. radiofrequency ablation: the CIRCA-DOSE trial. *Eur Heart J.* 2024;45:510–518. doi: 10.1093/eurheartj/ehad572
27. Andrade JG, Champagne J, Deyell MW, Essebag V, Lauck S, Morillo C, Sapp J, Skanes A, Theoret-Patrick P, Wells GA, et al; EARLY-AF Study Investigators. A randomized clinical trial of early invasive intervention for atrial fibrillation (EARLY-AF)—methods and rationale. *Am Heart J.* 2018;206:94–104. doi: 10.1016/j.ahj.2018.05.020
28. Andrade JG, Deyell MW, Badra M, Champagne J, Dubuc M, Leong-Sit P, Macle L, Novak P, Roux JF, Sapp J, et al. Randomised clinical trial of cryoballoon versus irrigated radio frequency catheter ablation for atrial fibrillation-the effect of double short versus standard exposure cryoablation duration during pulmonary vein isolation (CIRCA-DOSE): methods and rationale. *BMJ Open.* 2017;7:e017970. doi: 10.1136/bmjopen-2017-017970
29. Andrade JG, Khairy P, Verma A, Guerra PG, Dubuc M, Rivard L, Deyell MW, Mondesert B, Thibault B, Talajic M, et al. Early recurrence of atrial tachyarrhythmias following radiofrequency catheter ablation of atrial fibrillation. *Pacing Clin Electrophysiol.* 2012;35:106–116. doi: 10.1111/j.1540-8159.2011.03256.x
30. Sanders P, Purerfellner H, Pokushalov E, Sarkar S, Di Bacco M, Maus B, Dekker LR, Reveal LUI. Performance of a new atrial fibrillation detection algorithm in a miniaturized insertable cardiac monitor: results from the reveal LINQ usability study. *Heart Rhythm.* 2016;13:1425–1430. doi: 10.1016/j.hrthm.2016.03.005
31. Aguilar M, Macle L, Honfo SH, Khairy P, Cadrin-Tourigny J, Sidhu A, Deyell MW, Hawkins NM, Bennett RG, Andrade JG. Blanking period after catheter ablation of paroxysmal atrial fibrillation: insights from continuous cardiac monitoring. *Circ Arrhythm Electrophysiol.* 2025;18:e013232. doi: 10.1161/CIRCEP.124.013232