Left atrial appendage size is a marker of atrial fibrillation recurrence after radiofrequency catheter ablation in patients with persistent atrial fibrillation

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Abstract

Introduction Catheter ablation is an established therapy for rhythm control in patients with drug-refractory atrial fibrillation (AF), however, recurrence is frequent particularly in persistent AF. There are no consistently confirmed predictors of AF recurrence after catheter ablation. Therefore, we aimed to study whether LAA volume (LAAV) and function influence the long-term recurrence of AF after catheter ablation, depending on AF type. **Methods** AF patients who underwent point-by-point radiofrequency catheter ablation after cardiac computed tomography (CT) were included in this analysis. LAAV and LAA orifice area were measured by CT. Uni- and multivariable Cox proportional hazard regression models were performed to determine the predictors of AF recurrence. **Results** In total, 561 AF patients (61.9±10.2 years, 34.9% females) were included in the study. Recurrence of AF was detected in 40.8% of the cases (34.6% in patients with paroxysmal and 53.5% in those with persistent AF) with a median recurrence-free time of 22.7 [9.3-43.1] months. Patients with persistent AF had significantly higher iLAV, LAAV, LAA orifice area and lower LAA flow velocity, than those with paroxysmal AF. After adjustment left ventricular ejection fraction (LVEF) <50% (HR=2.17; 95%CI=1.38-3.43; p<0.001) and LAAV (HR=1.06; 95%CI=1.01-1.12; p=0.029) were independently associated with AF recurrence in persistent AF, while no independent predictors could be identified in paroxysmal AF. **Conclusion** The current study demonstrates that beyond left ventricular systolic dysfunction, LAA enlargement is associated with higher rate of AF recurrence after catheter ablation in persistent AF, but not in patients with paroxysmal AF.

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Short title

Predictors of atrial fibrillation recurrence

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Conflict of interest

The authors have no conflicts to disclose.

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Abstract

Introduction

Catheter ablation is an established therapy for rhythm control in patients with drug-refractory atrial fibrillation (AF), however, recurrence is frequent particularly in persistent AF. There are no consistently confirmed predictors of AF recurrence after catheter ablation. Therefore, we aimed to study whether LAA volume (LAAV) and function influence the long-term recurrence of AF after catheter ablation, depending on AF type.

Methods

AF patients who underwent point-by-point radiofrequency catheter ablation after cardiac computed tomography (CT) were included in this analysis. LAAV and LAA orifice area were measured by CT. Uni- and multivariable Cox proportional hazard regression models were performed to determine the predictors of AF recurrence.

Results

In total, 561 AF patients (61.9 ± 10.2 years, 34.9% females) were included in the study. Recurrence of AF was detected in 40.8% of the cases (34.6% in patients with paroxysmal and 53.5% in those with persistent AF) with a median recurrence-free time of 22.7 [9.3-43.1] months. Patients with persistent AF had significantly higher iLAV, LAAV, LAA orifice area and lower LAA flow velocity, than those with paroxysmal AF. After adjustment left ventricular ejection fraction (LVEF) $< 50\%$ (HR=2.17; 95%CI=1.38-3.43; $p < 0.001$) and LAAV (HR=1.06; 95%CI=1.01-1.12; $p = 0.029$) were independently associated with AF recurrence in persistent AF, while no independent predictors could be identified in paroxysmal AF.

Conclusion

The current study demonstrates that beyond left ventricular systolic dysfunction, LAA enlargement is associated with higher rate of AF recurrence after catheter ablation in persistent AF, but not in patients with paroxysmal AF.

Keywords

Atrial fibrillation; echocardiography, transesophageal; echocardiography, transthoracic; heart atria; recurrence; tomography, X-Ray

Abbreviations

AAD: anti-arrhythmic drug

AF: atrial fibrillation

BMI: body mass index

CAD: coronary artery disease

eGFR: estimated glomerular filtration rate

iLAV: body surface area-indexed left atrial volume

LA: left atrium

LAA: left atrial appendage

LAAV: left atrial volume

LVEF: left ventricular ejection fraction

PVI: pulmonary vein isolation

TIA: transient ischemic attack

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia.¹ It can lead to several health problems, such as heart failure, embolic events, and impaired quality of life. Moreover, it is associated with higher mortality rate.²⁻⁴ In case of drug-resistant symptomatic AF, catheter ablation proved to be an effective solution for rhythm control.⁵ However, depending on the ablation strategy and the type of AF, success rates of catheter ablation after 1 year vary considerably from 60% to 90%.⁵⁻⁷ Appropriate patient selection for catheter ablation is essential as neither AF recurrence nor procedural complication rates are negligible.⁸ However, there are no consistently confirmed predictors of AF recurrence following catheter ablation in the literature.⁹⁻¹⁸ It has been suggested that left atrial appendage (LAA) volume and function may be associated with the recurrence of AF/tachycardia in patients undergoing repeated ablation, the exact role of the LAA in the prediction of AF recurrence has not yet been resolved.¹⁹ The anatomy, including LAA volume, morphology and LAA orifice area can be accurately described using cardiac computed tomography (CT), and LAA function can be assessed by measuring LAA flow velocity using transesophageal echocardiography (TEE).

We aimed to study the role of LAA volume (LAAV), and function in the success of catheter ablation by type of AF.

Methods

Study population

In our multimodality retrospective study, we included consecutive patients with symptomatic AF who underwent initial point-by-point radiofrequency catheter ablation at the Heart and Vascular Center of Semmelweis University, Budapest, Hungary between January 2014 and December 2017. All patients underwent preprocedural cardiac CT for the assessment of left atrial (LA) anatomy. LAA function was assessed with LAA flow velocity measured by TEE. Left ventricular ejection fraction (LVEF) was measured by transthoracic echocardiography. Exclusion criteria were age under 18 years, non-diagnostic CT image quality, history of prior pulmonary vein isolation or heart surgery, and missing echocardiography data on LAA flow velocity. Due to the retrospective analysis of clinically acquired data, the institutional review board waived the need for written patient informed consent. The study was performed according to the Declaration of Helsinki and Institutional Guidelines.

Cardiac CT imaging

CT examinations were performed with a 256-slice scanner (Brilliance iCT 256, Philips Healthcare, Best, The Netherlands) with prospective ECG-triggered axial acquisition mode. 100-120 kV with 200-300 mAs tube current was used depending on patient anthropometrics. Image acquisition was performed with 128x0.625 mm detector collimation, and 270 msec gantry rotation time. For heart rate control 50-100 mg metoprolol was given orally and 5-20 mg intravenously, if necessary. In total 85-95 ml contrast material (Iomeron 400, Bracco Ltd, Milan, Italy) was injected with a flow rate of 4.5-5.5 ml/sec via antecubital vein access using a four-phasic injection protocol.²⁰ Bolus tracking in the LA was used to obtain proper scan timing. All patients received 0.8 mg sublingual nitroglycerin between the native CT and CTA examinations. CT data sets were reconstructed with 0.8 mm slice thickness and 0.4 mm increments. The LA and LAA volumes were measured using a semiautomatic software tool (EP Planning, Philips IntelliSpace Portal, Philips Healthcare, Best, The Netherlands) and if needed the borders of LA and LAA, the orifices of the pulmonary veins and the level of the mitral valve were manually adjusted.

LAA flow velocity measurement

Maximum 24h before ablation, all patients underwent TEE examination to exclude the presence of LAA thrombus. iE33 and Epiq 7C (Philips Medical System, Andover, MA) systems equipped with S5-1 phased array and X7-2t matrix TEE transducers were used. TEE was performed during conscious sedation. The LAA was imaged from 0°, 45°, 90° and 135° views to detect spontaneous echo contrast, sludge or thrombus. Subsequently, a sample volume was placed at the middle portion of the LAA and the peak velocity of the outflow of the LAA was measured.

Catheter ablation procedure

The indications for AF ablation procedures were in accordance with the current guidelines.^{1, 21} Paroxysmal AF was defined as self-terminating AF, in most cases within 48 hours. Some AF paroxysms continued up to 7 days.²¹ Persistent AF was defined as AF that lasts longer than 7 days.²¹ Conscious sedation was carried out in all cases with intravenous fentanyl, midazolam, and propofol. Basic vital parameters of the patients were monitored in all cases with non-invasive blood pressure measurements every 10 minutes and continuous pulse oximetry. Femoral venous access was used for all procedures. Transseptal puncture was performed routinely with fluoroscopy guidance and pressure monitoring, while intracardiac echocardiography was also utilized in difficult cases. All ablations were performed with the support of an electroanatomical mapping system (either CARTO, Biosense Webster, Inc., Diamond Bar, CA, USA; or ENSITE, St. Jude Medical, Inc., MN, USA), and the LA fast anatomical map was fused with the cardiac CT images to guide ablation (temperature-controlled mode, 43degC, 25–35 W, irrigated 4 mm tip catheter) in the majority of patients. Pulmonary vein isolation was performed in each patient. Moreover, in patients with long-standing persistent AF, additional ablation lines were drawn at the discretion of the operating physician. All patients without complications were discharged the day after the procedure.

Follow-up and definition of AF recurrence

After discharge, outpatient clinical follow-up visits were scheduled at 3, 6, 12 months after the procedure and at least once yearly thereafter. The follow-up visits included clinical assessment of the patient and 24-hour Holter ECG monitoring. Follow-up data were registered in the structured reporting platform (Axis, Neumann Medical Ltd, Budapest, Hungary). Recurrence of AF was defined as the occurrence of atrial tachyarrhythmia that lasted for more than 30 sec.^{1, 21} AF recurrences during the first 90 days after catheter ablation were not included in order to exclude AF during this vulnerable „blanking period”, which might be only a temporary phenomenon due to the inflammation, maturation and healing of the ablated lesions.^{22, 23}

Statistical analysis

Categorical variables are expressed as frequencies (percentages) and continuous values are expressed as mean±standard deviation (SD). Normality of continuous parameters was tested with Shapiro-Wilk test. Tests for significance were conducted using Mann-Whitney-Wilcoxon or Kruskal-Wallis tests for continuous variables and Pearson’s chi-square or Fisher exact tests (in case of 5 or less observations) for categorical

variables. The event-free survival rate was estimated using Kaplan-Meier method and log-rank test was applied for the comparisons between the various groups. Cumulative event rates were calculated with event or censoring times measured from the date of ablation. For patients who did not experience AF recurrence, their time-to-event measure was censored at the last follow-up visit date.

To identify parameters associated with AF recurrence after catheter ablation, uni- and multivariate Cox proportional hazard regression model was executed. In the multivariate model, adjustment was made for age >65 years, persistent AF, impaired eGFR (<60 ml/min/1.73 m²), body surface area-indexed LA volume (iLAV) measured by CT, LVEF <50%, sex, obesity (defined as body mass index ≥ 30 kg/m²), hypertension, dyslipidemia, diabetes (Type I and II), prior stroke/transient ischemic attack (TIA), obstructive coronary artery disease (CAD), thyroid gland diseases (hypo- and hyperthyroidism), unsuccessful preablation anti-arrhythmic drug (AAD) therapy (including sotalol, propafenone and amiodarone therapies), and LAAV. Thirty patients were randomly selected for interobserver agreement and analyzed using intraclass correlation coefficient (ICC). Relative risks were expressed as hazard ratios (HRs) with associated 95% confidence intervals (CIs). Two-tailed p values smaller than 0.05 were considered significant. All statistical analyses were performed in R environment (version 3.6.1). Cox proportional hazard regression analysis was done using the 'survival' package (version 3.1-8). Kaplan-Meier curve and log-rank test were performed using the 'survminer' (version 0.4.6).

Results

Patient characteristics

A total of 561 patients were included in the current analysis. Mean age was 61.9±10.2 years and 34.9% of the patients were female. Recurrence of AF was reported in 40.8% of the patients (34.6% in patients with paroxysmal and 53.5% in those with persistent AF). Median recurrence-free time was 22.7 [9.3-43.1] months (21.8 [9.4-43.2] months in paroxysmal and 23.6 [9.0-42.6] months in persistent AF). An excellent interobserver agreement was obtained for both the iLAV (ICC=0.99), and LAAV (ICC=0.90) measurements. The proportion of individuals aged >65 years (40.7% vs 49.3%; $p=0.046$), female gender (30% vs 41.9%; $p=0.005$), persistent AF (25.9% vs 43.2%; $p<0.001$), and LVEF <50% (6.9% vs 21.0%; $p<0.001$) were significantly higher in patients with AF recurrence. Moreover, patients with AF recurrence had significantly higher iLAV (54.4±19.3 ml/m² vs 61.8±23.9 ml/m²; $p<0.001$), LAAV (7.6±3.2 ml vs 8.8±5.2 ml; $p=0.002$) and LAA orifice area (387.6±140.5 mm² vs 454.4±167.7 mm²; $p<0.001$). Anthropometric data, cardiovascular comorbidities, AAD therapy and imaging parameters are summarized in Table 1. Medications and procedural times are reported in Supplementary table 1.

We also examined the differences of the clinical and imaging parameters between patients with paroxysmal and persistent AF. Those patients with persistent AF had significantly higher proportion of age >65 years (41.0% vs 50.8%; $p=0.030$), hypertension (67% vs 85.9%; $p<0.001$) and LVEF <50% (6.6% vs 24.9%; $p<0.001$). Regarding the CT parameters, we measured significantly higher iLAV (51.0±15.9 ml/m² vs 70.4±25.6 ml/m²; $p<0.001$), LAAV (7.4±3.0 ml vs 9.5±5.6 ml; $p=0.002$), LAA orifice area (385.2±132.8 mm² vs 475.2±179.7 mm²; $p<0.001$) and lower LAA flow velocity (35.3±13.4 cm/sec vs 31.7±12.0 cm/sec; $p<0.001$). Detailed data on the clinical and imaging parameters by AF type can be seen in Table 2 and Figure 1.

Predictors of AF recurrence

Significantly higher iLAV and LAAV values were measured in patients with persistent AF recurrences, and larger LAA orifice area values were measured both in paroxysmal and persistent recurrences, as reported in Figure 1. To explore the associations between the various examined parameters and AF recurrence, Cox proportional hazards regression analyses were performed, as stratified by AF type. In the univariate analysis, female sex (HR=1.43; 95%CI=1.01-2.02; $p=0.043$) was significantly associated with AF recurrence in patients with paroxysmal AF, while in those with persistent AF LVEF <50% (HR=2.07; 95%CI=1.36-3.14; $p<0.001$), iLAV (HR=1.01; 95%CI=1.00-1.02; $p=0.027$), LAAV (HR=1.07; 95%CI=1.03-1.10; $p<0.001$) and LAA orifice area (HR=1.02; 95%CI=1.00-1.03 per 10 mm²; $p=0.005$) showed an association with AF

recurrence.

After adjustment LVEF <50% (HR=2.17; 95%CI=1.38-3.43; p<0.001) and LAAV (HR=1.06; 95%CI=1.01-1.12; p=0.029) remained a significant predictor of AF recurrence in patients with persistent AF, while in paroxysmal AF no independent predictors could be identified in the multivariate analysis. Detailed results of the uni- and multivariate Cox regression analyses are reported in Table 3. Kaplan-Meier curves of AF recurrence-free survival in persistent AF stratified by LVEF and LAAV can be seen in Figure 2.

Discussion

We demonstrated that beyond impaired LVEF, a larger LAAV is an independent predictor of AF recurrence after catheter ablation in patients with persistent AF. Interestingly, this association was not present in patients with paroxysmal AF.

AF is a complex disease with incompletely understood mechanisms. Although significant progress has been made in the last two decades, the efficacy of ablation therapy remains suboptimal, particularly in persistent AF. One-year success rate of catheter ablation varies between 60 and 90%.⁵⁻⁷ Previous studies have shown that the majority of AF recurrence occurred in the first two years after catheter ablation.²⁴ So far, persistent AF, LA enlargement, hypertension, diabetes mellitus, aging, obesity, heart failure, chronic renal insufficiency and preprocedural amiodarone failure have been reported as independent predictors of AF recurrence.^{1, 21, 24-27} However, the data are controversial and the conclusions of previous studies are inconsistent. Several studies aimed to investigate the role of different scoring systems in the prediction of rhythm outcomes after AF ablation. While the HATCH score was found to have no value in the prediction of AF recurrence after catheter ablation, R₂CHADS₂ and CHA₂DS₂-VASc scores were associated with rhythm outcomes.^{28, 29} Since APPLE score proved to be superior to the CHA₂DS₂-VASc score for the prediction of rhythm outcome after catheter ablation, we incorporated its factors into our multivariable models.³⁰ Due to inconsistent definition of recurrence, estimation of the AF ablation success is challenging.^{1, 21} Current guidelines of the European Society of Cardiology define AF recurrence as the occurrence of atrial tachyarrhythmia that last for more than 30 sec.^{1, 21} In the current study, we have also applied this definition. Moreover, previous studies have reported a wide range of recurrent AF duration time following various ablation strategies. In our study, we included AF patients who underwent point-by-point catheter ablation procedure after 2014 in order to provide more useful information to the current clinical practice. Moreover, since efficacy of radiofrequency catheter ablation varies greatly between paroxysmal and persistent AF, we analyzed the outcomes separately by type of AF. Since radiofrequency catheter ablation procedure became more widely performed, clinical studies regarding the long-term effectiveness are important, especially in patients with persistent AF. In our study population the recurrence rate after point-by-point catheter ablation was 53.5% in persistent AF and 34.6 in paroxysmal AF after a single procedure. These findings suggest that catheter ablation in patients with persistent AF should be chosen very cautiously due to the low success rate and non-negligible complication rate. In the present study, left ventricular systolic dysfunction and higher LAAV were identified as significant predictors of AF recurrence in patients with persistent AF who underwent point-by-point catheter ablation.

Di Biase et al have reported that LAA appears to be responsible for recurrence of AF/tachycardia in at least 27% of patients undergoing repeated ablation, especially in persistent AF cases.¹⁹ Moreover, electric isolation of the LAA was associated with an improved AF-free/recurrence-free survival.³¹ Despite the increasing evidence of the role of LAA in triggering atrial arrhythmias, the literature is scarce regarding the contributing factors. Previous smaller studies including both paroxysmal and persistent AF patients undergoing catheter ablation have shown that larger LAAV is associated with a higher risk of AF recurrence.^{32, 33} The LAA is known to be more compliant than the LA, and therefore may play an important role in the modulation of LA pressure and LAAV measurement could be a reliable tool in determining the structural and functional conditions of LA from the early stage of AF.³⁴ In line with these findings, our results also suggest that LAAV may be a surrogate of increased LAA arrhythmogenicity. LAA has a complex anatomy and LAA enlargement might result in longer activation pathways and development of re-entry through interstitial fibrosis.³⁵

The current study has several limitations. First, it was a single-center, retrospective study, therefore the results need further validation in prospective, multi-center studies. Second, even if patients were closely followed-up with regular clinical visits, ECG and Holter monitoring, asymptomatic AF episodes might have happened between two visits. Moreover, ablation strategy was not uniform in all subjects, as additional ablations were permitted beyond PVI if operator decided to draw additional lines.

Conclusion

Despite advances in catheter ablation techniques, AF recurrence rate is relatively high. The current study demonstrates that beyond left ventricular systolic dysfunction, LAA enlargement is an independent predictor of AF recurrence after catheter ablation in persistent AF. Our results suggest that preprocedural assessment of LVEF and LAAV might contribute to optimal patient selection and aid to improve long-term results of ablation procedures in patients with persistent AF.

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Figures

Figure 1. Comparison of LA and LAA parameters between patients with and without AF recurrence stratified by AF type

Abbreviations: AF = atrial fibrillation; iLAV = body surface area-indexed left atrial volume; LAA = left atrial appendage.

Figure 2. AF recurrence-free survival according to LVEF and LAAV in patients with persistent AF

Abbreviations: AF = atrial fibrillation; LAAV = left atrial appendage volume; LVEF = left ventricular ejection fraction.

Tables

Table 1. Patient characteristics

	All patients (n=561)	No AF recurrence (n=332)
Anthropometric data and comorbidities	Anthropometric data and comorbidities	Anthropometric data and comorbidities
Age > 65 years, n (%)	248 (44.2)	135 (40.7)
Female, n (%)	561 (34.9)	100 (30.1)
Persistent AF, n (%)	185 (33.0)	86 (25.9)
Obesity, n (%)	187 (33.3)	112 (33.7)
Hypertension, n (%)	411 (73.3)	238 (71.7)
Hyperlipidemia, n (%)	143 (25.5)	86 (25.9)
Diabetes, n (%)	82 (14.6)	50 (15.1)
Obstructive CAD, n (%)	51 (9.1)	28 (8.4)
Stroke/TIA, n (%)	43 (7.7)	27 (8.1)
Thyroid gland disease, n (%)	56 (10.0)	36 (10.8)
eGFR < 60 ml/min/1.73 m ²	138 (24.6)	83 (25.0)
Imaging parameters	Imaging parameters	Imaging parameters
LVEF $< 50\%$, n (%)	71 (12.7)	23 (6.9)
iLAV (ml/m ²)	57.4 $\pm$ 21.6	54.4 $\pm$ 19.3
LAAV (ml)	8.1 $\pm$ 4.2	7.6 $\pm$ 3.2
LAA orifice area (mm ²)	414.9 $\pm$ 155.6	387.6 $\pm$ 140.5
LAA flow velocity (cm/sec)	34.1 $\pm$ 13.0	34.1 $\pm$ 13.2

Abbreviations: AAD = anti-arrhythmic drug; AF = atrial fibrillation; CAD = coronary artery disease; eGFR = estimated glomerular filtration rate; iLAV = body surface area-indexed left atrial volume; LAA = left atrial appendage; LAAV = left atrial volume; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.

Supplementary table 1.

Medications

NOAC, n (%)	312 (55.6)
OAC, n (%)	237 (42.2)
Syncumar, n (%)	74 (13.2)
Warfarin, n (%)	121 (21.6)
Dabigatran, n (%)	113 (20.1)
Rivaroxaban, n (%)	100 (17.8)
LMWH, n (%)	251 (44.7)
Antiplatelet therapy, n (%)	13 (2.3)
Apixaban, n (%)	24 (4.3)
AAD therapy, n (%)	283 (50.4)
Sotalol, n (%)	47 (8.4)
Amiodarone, n (%)	139 (24.8)
Propafenon, n (%)	97 (17.3)
Procedural times	Procedural times
Procedure time (min)	94.7±28.1
LA time (min)	64.8±23.5
Fluoroscopy time (min)	9.7±6.5

Abbreviations: LA = left atrium; LMWH = light molecular weight heparin; NOAC = non-Vitamin K antagonist oral anticoagulation; OAC = oral anticoagulant.

Table 2. Clinical characteristics by AF type

	Paroxysmal AF (n=376)	Persistent AF (n=185)	p
Age>65 years, n (%)	154 (41.0)	94 (50.8)	0.030
Female, n (%)	136 (36.2)	60 (32.4)	0.398
Obesity, n (%)	132 (35.1)	55 (29.7)	0.217
Hypertension, n (%)	252 (67.0)	159 (85.9)	<0.001
Hyperlipidemia, n (%)	86 (22.9)	57 (30.8)	0.050
Diabetes, n (%)	49 (13.0)	33 (17.8)	0.162
Obstructive CAD, n (%)	34 (9.0)	17 (9.2)	1.000
Stroke/TIA, n (%)	32 (8.5)	11 (5.9)	0.316
Thyroid gland disease, n (%)	46 (12.2)	10 (5.4)	0.011
eGFR<60 ml/min/1.73 m ²	100 (26.6)	38 (20.5)	0.144
Pre-ablation AAD therapy, n (%)	196 (52.1)	87 (47.0)	0.281
LVEF<50%, n (%)	25 (6.6)	46 (24.9)	<0.001

Abbreviations: AAD = anti-arrhythmic drug; AF = atrial fibrillation; CAD = coronary artery disease; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.

Table 3. Associates of AF recurrence in patients with paroxysmal AF

	Paroxysmal AF	Paroxysmal AF	Paroxysmal AF	Paroxysmal AF
	Unadjusted analysis	Unadjusted analysis	Unadjusted analysis	Adjusted analysis
	HR	95%CI	p	HR

	Paroxysmal AF	Paroxysmal AF	Paroxysmal AF	Paroxysmal AF
Age>65 years, n (%)	1.01	0.71-1.42	0.967	1.02
Female, n (%)	1.43	1.01-2.02	0.043	1.42
Obesity, n (%)	1.08	0.75-1.54	0.685	1.09
Hypertension, n (%)	0.96	0.66-1.39	0.816	0.91
Hyperlipidemia, n (%)	0.82	0.54-1.24	0.338	0.86
Diabetes, n (%)	0.77	0.45-1.33	0.353	0.79
Obstructive CAD, n (%)	1.08	0.62-1.89	0.781	1.28
Stroke/TIA, n (%)	0.88	0.47-1.62	0.673	0.96
Thyroid gland disease, n (%)	0.94	0.55-1.58	0.806	0.85
eGFR<60 ml/min/1.73 m ²	1.38	0.93-2.06	0.111	1.30
Pre-ablation AAD therapy, n (%)	0.96	0.68-1.36	0.836	1.00
LVEF<50%, n (%)	1.67	0.96-2.91	0.069	1.42
iLAV (ml/m ²)	1.01	0.99-1.02	0.098	1.01
LAAV (ml)	1.03	0.97-1.09	0.325	1.00
LAA orifice area (mm ²), per 10 mm ²	1.01	1.00-1.03	0.034	1.00
LAA flow velocity (cm/sec)	1.00	0.99-1.03	0.352	1.01

Abbreviations: AAD = anti-arrhythmic drug; AF = atrial fibrillation; BMI = body mass index; CAD = coronary artery disease; iLAV = body surface area-indexed left atrial volume; LAA = left atrial appendage; LAAV = left atrial volume; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.