

# Association of left atrial enlargement and increased left ventricular wall thickness with arrhythmia recurrence after cryoballoon ablation for atrial fibrillation

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## ABSTRACT

**Background:** Left atrial enlargement (LAE) predicts atrial fibrillation (AF) recurrence after cryoballoon-based pulmonary vein isolation (CB). Increased left ventricular wall thickness (LVWT) is pathophysiologically associated with LAE and atrial arrhythmias.

**Aims:** To assess effect of increased LVWT on long-term outcomes of CB depending on coexistence of LAE.

**Methods:** LAE was defined using either echocardiography ( $>48 \text{ cm}^3/\text{m}^2$ ) or multislice computer tomography (MSCT,  $\geq 63 \text{ cm}^3/\text{m}^2$ ). Increased LVWT was echocardiographic septal/posterior wall thickness  $>10 \text{ mm}$  in males and  $>9 \text{ mm}$  in females. All patients achieved 2-year follow-up.

**Results:** Of 250 patients (median [interquartile range, IQR] age of 61 [49.0–67.3] years; 30% female) with AF (40% non-paroxysmal), 66.5% had hypertension, and 27.2% underwent redo procedure. MSCT was done in 76%. During follow-up of 24.5 (IQR, 6.0–31.00) months the clinical success rate was 72%, despite 46% of patients having arrhythmia recurrence. Arrhythmia recurrence risk was increased by LAE and increased LVWT (hazard ratio [HR], 1.801;  $P = 0.002$  and HR, 1.495;  $P = 0.036$ ; respectively). The highest arrhythmia recurrence (61.9% at 2 years) was among patients with LAE and increased LVWT (33.6% of patients); intermediate (41.8%) among patients with isolated LAE; and lowest among patients with isolated increased LVWT or patients without LAE or increased LVWT (36.8% and 35.2% respectively,  $P = 0.004$ ). After adjustment for body mass index (BMI), paroxysmal AF, CHA<sub>2</sub>DS<sub>2</sub>-VASc score, clinically-significant valvular heart disease, and cardiomyopathy, patients with LAE and concomitant increased LVWT diagnosis had a 1.8-times increased risk of arrhythmia recurrence (HR, 1.784; 95% confidence interval [CI], 1.017–3.130;  $P = 0.043$ ).

**Conclusion:** Joint occurrence of LAE and increased LVWT is associated with the highest rate of arrhythmia recurrence after CB for AF.

**Key words:** arrhythmia recurrence, atrial fibrillation, catheter ablation, cryoballoon, pulmonary vein isolation

## WHAT'S NEW?

Cryoballoon-based pulmonary vein isolation (CB) for atrial fibrillation (AF) can be effective for maintaining sinus rhythm in many patients. This analysis assesses the effect of increased left ventricular wall thickness (LVWT) on long-term outcomes of CB depending on the coexistence of left atrial enlargement (LAE). The analysis was done in a real-life scenario in consecutive patients in a tertiary center. LAE in the setting of increased LVWT substantially increased the arrhythmia recurrence rate after CB for AF.

## INTRODUCTION

Cryoballoon-based (CB) pulmonary vein isolation is an effective option for rhythm control in atrial fibrillation (AF) [1]. Having the ability to predict post-procedural AF recurrence would have a great impact on procedural planning, costs to the health care system, and patient outcomes. There have been multiple attempts to predict the recurrence of AF utilizing different risk factors and risk scores with moderate results [2, 3]. Left atrial (LA) enlargement (LAE), which is associated with the progression of structural remodeling and fibrosis of LA tissues, affects catheter ablation outcomes [2, 4]. The American and European Cardiology Society guidelines recommend measuring left atrial volume index as a reliable indicator of LA size [5]. Multislice computed tomography (MSCT) may be more accurate and operator-independent, offering higher visual resolution than two-dimensional (2D) echocardiography [6].

Increased left ventricular wall thickness (LVWT), leading to diastolic dysfunction and elevation of cardiac filling pressures, can lead to LAE [7]. Increased LVWT is associated with an increased rate of AF recurrence [8]. Left ventricular (LV) hypertrophy, with its increased LVWT prerequisite, was shown to be associated with the development of atrial arrhythmias, particularly AF [9], and the prevalence of AF is higher in patients with hypertrophic remodeling [10]. The purpose of this article is to assess the combined predictive value of LAE and increased LVWT for AF recurrence after CB ablation.

## METHODS

### Study population

This is a single-center retrospective study of 250 consecutive patients with AF who underwent CB for *de novo* or redo procedures of AF between May 2017 and April 2019. All patients were qualified for CB according to the current European guidelines [1].

Based on the presence of LAE and increased LVWT, the patients were divided into four study groups: (1) neither increased LVWT nor LAE (increased LVWT [-]LAE[-] group); (2) patients with increased LVWT only (increased LVWT [+] LAE[-] group); (3) patients with isolated LAE (increased LVWT [-]LAE[+] group), and (4) patients with LAE concomitant with increased LVWT (increased LVWT [+]LAE[+] Group). LAE was defined using either baseline echocardiography ( $>48 \text{ cm}^3/\text{m}^2$ ) [5] or MSCT ( $\geq 63 \text{ cm}^3/\text{m}^2$ ) [11].

Increased LVWT was echocardiographic septal/posterior wall thickness  $>10 \text{ mm}$  in males and  $>9 \text{ mm}$  in females [5].

As the present study was a retrospective analysis of previously obtained data, and the patients were treated routinely with the best current practice, the institutional ethics committee approval did not require patient-signed informed consent. Relevant data were extracted from the electronic medical records stored at our institution.

### Cryoballoon ablation procedure

Ablation was performed under conscious sedation. Via femoral venous access, a quadripolar catheter was placed in the coronary sinus. LA access was obtained by a transseptal puncture. Intravenous heparin was administered before and during ablation with a targeted activated clotting time of  $\geq 300$  seconds. A dedicated 15F delivery sheath (FlexCath; Medtronic Inc, Minneapolis, MN, US) was introduced into the LA over-the-wire. A 23- or 28-mm diameter cryoballoon was advanced through the FlexCath sheath into the LA and placed into the antrum of the pulmonary vein (PV) with a dedicated inner lumen mapping catheter (Achieve; Medtronic). The inflated cryoballoon was advanced towards the antral surface of the PV, and adequate PV occlusion with the balloon was determined by injection of a radiopaque contrast agent through the distal end of the catheter. The inner lumen circular mapping catheter was used, the electrodes were positioned as closely as possible to the PV antrum to monitor for PV isolation, and cryoapplication was initiated. The cryoballoon application time was the recommended 120 seconds from isolation of the PV, up to 240 seconds per ablation; however, the number and duration of cryoapplications were according to physician preference. Phrenic nerve pacing was conducted using a diagnostic catheter at the level of the right subclavian vein during right-sided PV ablation, and diaphragmatic movement was monitored. Cryoapplication was immediately terminated upon weakened diaphragmatic response. Systemic anticoagulation was recommended for at least 3 months after the procedure.

### Left ventricular thickness and LA volume measurements

Before the CB procedure, all patients underwent two-dimensional transthoracic echocardiography (2D-echo; GE Vivid E95, General Electric, Boston, MA, US) with evaluation of LV ejection fraction (LVEF) and LV wall thickness. To assess

PV variants (common/accessory veins) and to exclude LA thrombus, all patients underwent either transesophageal 2D echocardiography (GE Vivid E95) or contrast-enhanced ECG-gated MSCT (384-slice SOMATOM Definition Flash, Dual Source, Siemens Healthcare GmbH, Erlangen, Germany), depending on their availability. Both 2D echocardiography (2D-echo) and MSCT acquired images were recorded for offline analysis, using EchoPAC™ version 204 (General Electric) or syngo.via (Siemens Healthcare GmbH), respectively. The 2D-echo LV wall thickness and maximum LA volume were measured as recommended [5]. The 2D-echo LA volumes were measured at the end of LV systole considering the mitral annulus as an LA atrioventricular border, using the modified biplane Simpson's disc summation method [12]. Using the MSCT, LA volume was calculated automatically (syngo.via) by a modified Simpson's method after manual tracing of the endocardial borders in the 10–20 sequential/successive LA cross-sections at LV end-systole in oblique sagittal and long-axis MSCT angiograms [13]. Maximal LA volume was defined at LV end-systole just before mitral valve opening, with the mitral annulus being the LA atrioventricular border. Measured LA volumes were indexed for corresponding body surface area calculated using the DuBois and DuBois formula [14].

### Definitions

Concomitant clinically relevant valvular heart disease (VHD) was diagnosed on echocardiography as severe mitral or tricuspid insufficiency (MI/TI) or a history of any artificial valve replacement. Cardiomyopathy (CM) risk factors included dilated (DCM), hypertrophic (HCM), ischemic (ICM) or arrhythmogenic right ventricular dysplasia, CHA<sub>2</sub>DS<sub>2</sub>-VASc — Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65–74 years, Sex category (female). Significant clinical improvement is associated with European Heart Rhythm Association (EHRA) scale reduction of at least 1 point assuming that the EHRA score is not greater than II.

### Follow-up assessment

Observation was based on planned visits to the outpatient clinic or telephone interviews. The primary endpoint of the study was recurrence of any atrial arrhythmia lasting more than 30 seconds on ECG-Holter monitoring, implantable cardiac device memory, telemetry in emergency departments, or arrhythmia recorded on standard 12-lead ECG. The first 3 months post-ablation were considered a blanking period during which the primary endpoint could not be reached. All patients were followed for at least 2 years after ablation.

### Statistical analysis

Using the Shapiro-Wilk test, the hypothesis of normal distribution was rejected in all of the studied continuous variables, and they have been presented as median with interquartile range (IQR). Categorical variables have been

presented as frequencies and percentages. Differences between continuous variables were determined as appropriate either by the Mann-Whitney or Kruskal-Wallis tests, and Wilcoxon for paired variables. Differences between categorical variables were determined by Fisher's exact test. Prognostic values of increased LVWT and LAE were analyzed in a multivariable Cox regression model adjusted for the relevant clinical data with a well-established prognostic value and associated with cardiac remodeling (BMI, paroxysmal AF, CHA<sub>2</sub>DS<sub>2</sub>-VASc score, VHD, and CM) [15–17]. We calculated respective hazard ratios (HR) and corresponding 95% confidence intervals (CI). Kaplan-Meier curves were compared with the log-rank test.  $P < 0.05$  was considered statistically significant. All statistical analyses were performed using the PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, US).

## RESULTS

### Study population

There were 250 patients treated with CB at median age of 61 years (IQR 49.0–67.3 years; minimum 23 years — maximum 81 years). The majority were male (70.0%). Most had paroxysmal AF (60.4%,  $n = 151$ ); 22.0% ( $n = 55$ ) had persistent and 17.6% ( $n = 44$ ) long-persistent AF. The median EHRA score was II (II–III), and the CHA<sub>2</sub>DS<sub>2</sub>-VASc score was 2.0 (1.0–3.0). CB was a redo procedure in 27.2% ( $n = 68$ ) of patients. VHD was present in 4.8% ( $n = 12$ ) and CM in 17.2% ( $n = 43$ ), and 38 patients (15.2%) had coronary artery disease. LVEF <60% was found in 29.6% ( $n = 74$ ), and 11 patients (4.4%) had implanted cardiac resynchronization therapy (CRT)/an implantable cardioverter defibrillator (ICD).

### Anatomy and study groups

Median LA indexed volume was bigger among patients examined with MSCT (76%) than using 2D-echo (64.8 [54.3–78.6] vs. 55.9 [39.6–72.5] cm<sup>3</sup>/m<sup>2</sup>;  $P = 0.001$ ); however, LAE was diagnosed with similar frequency using the two modalities (53.2% vs. 63.3%;  $P = 0.18$ ). Increased LVWT was seen in 56.4% ( $n = 141$ ), with median thickness of septal and posterior wall being 11.5 mm (11.0–12.8) and 11.0 mm (9.3–11.0) among females and 12.0 mm (11.0–13.0) and 11.0 mm (10.4–12.0) in males. LAE was of similar frequency among patients with and without increased LVWT (59.6% vs. 50.5%,  $P = 0.16$ ). Overall, 21.6% of patients had neither increased LVWT nor LAE ( $n = 54$ ), 22.8% ( $n = 57$ ) had only increased LVWT, and 22.0% ( $n = 55$ ) had isolated LAE. In 84 patients (33.6%), there was concomitant LAE and increased LVWT.

**Table 1** displays a comparison of baseline characteristics among the studied groups. Patients with LAE were older and had more persistent/long-persistent (vs. paroxysmal) AF. Patients with increased LVWT were more often men and had a higher CHA<sub>2</sub>DS<sub>2</sub>-VASc score and more hypertension. The increased LVWT (+)LAE(+) group had a high prevalence of cardiomyopathy (almost a third of patients)

**Table 1.** Comparison of demographic and baseline clinical characteristics among the studied groups stratified according to LAE and increased LVWT

	↑LVWT(-) LAE(-) (n = 54, 21.6%)	↑LVWT(+) LAE(-) (n = 57, 22.8%)	↑LVWT(-) LAE(+) (n = 55, 22.0%)	↑LVWT(+) LAE(+) (n = 84, 33.6%)	P-value
Age, years, median (IQR)	58.5 (41.0–66.0)	59.0 (47.5–65.0)	62.0 (56.0–67.0) <sup>a</sup>	63.0 (54.0–71.0) <sup>a</sup>	0.006
BMI, kg/m <sup>2</sup> , median (IQR)	27.4 (25.0–29.1)	27.8 (25.5–30.5)	27.2 (25.0–28.9)	27.8 (25.7–30.6)	0.30
Female, n (%)	26 (48.1)	10 (17.5) <sup>a</sup>	20 (36.4)	19 (22.6) <sup>a</sup>	0.001
EHRA score, median (IQR)	2.0 (2.0–3.0)	2.0 (2.0–3.0)	2.0 (2.0–3.0)	2.0 (2.0–3.0)	0.84
CHA <sub>2</sub> DS <sub>2</sub> -VASc, median (IQR)	1.0 (0.0–2.0)	2.0 (1.0–3.0)	1.0 (1.0–3.0)	2.0 (1.0–3.0) <sup>a</sup>	0.03
Paroxysmal AF, n (%)	44 (81.5)	42 (73.7)	29 (52.7) <sup>a</sup>	36 (42.9) <sup>a</sup>	<0.001
Persistent AF, n (%)	6 (11.1)	13 (22.8)	8 (14.5)	28 (33.3) <sup>a</sup>	0.008
Long-persistent AF, n (%)	4 (7.4)	2 (3.5)	18 (32.7) <sup>a</sup>	20 (23.8) <sup>a</sup>	<0.001
Redo CB, n (%)	14 (25.9)	15 (26.3)	15 (27.3)	24 (28.6)	0.99
DM, n (%)	5 (9.3)	5 (8.8)	4 (7.3)	7 (8.3)	0.99
Hypertension, n (%)	29 (53.7)	44 (77.2) <sup>a</sup>	33 (60.0)	63 (75.0) <sup>a</sup>	0.01
CAD, n (%)	5 (9.3)	12 (21.1)	5 (9.1)	16 (19.0)	0.14
Stroke/TIA, n (%)	0 (0)	6 (10.5) <sup>a</sup>	5 (9.1)	11 (13.1) <sup>a</sup>	0.06
Baseline eGFR, ml/min/1.73m <sup>2</sup> , median (IQR)	66.8 (60.0–85.7)	72.5 (60.0–90.0)	67.3 (60.0–82.0)	68.9 (60.0–81.1)	0.78
Prior pacemaker, n (%)	2 (3.2)	4 (6.2)	3 (6.4)	4 (5.3)	0.86
ICD/CRT, n (%)	2 (3.7)	2 (3.5)	1 (1.8)	6 (7.1)	0.47
Overall CM, n (%)	4 (7.4)	8 (14.0)	7 (12.7)	24 (28.6) <sup>a</sup>	0.006
ICM, n (%)	1 (1.9)	2 (3.5)	0 (0)	6 (7.1)	0.14
DCM, n (%)	1 (1.9)	4 (7.0)	7 (12.7)	9 (10.7)	0.14
HCM, n (%)	0 (0)	2 (3.5)	0 (0)	9 (10.7)	0.004
ARVD, n (%)	2 (3.7)	0 (0)	0 (0)	0 (0)	0.06
Overall VHD, n (%)	1 (1.9)	1 (1.8)	4 (7.3)	6 (7.1)	0.27
Follow-up period, months, median (IQR)	28.5 (6.8–33.0)	27.1 (10.0–32.5)	26.0 (6.0–31.0)	12.0 (3.0–26.8)	<0.001

<sup>a</sup>P < 0.05 for difference in comparison to the reference group (↑LVWT [-]LAE[-])

Abbreviations: AF, atrial fibrillation; ARVD, arrhythmogenic right ventricular dysplasia; BMI, body mass index; CAD, coronary artery disease; CB, cryoballoon-based pulmonary vein isolation; CHA<sub>2</sub>DS<sub>2</sub>-VASc, Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65–74 years, Sex category (female); CM, cardiomyopathy; CRT, cardiac resynchronization therapy; DCM, dilative cardiomyopathy; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; EHRA, European Heart Rhythm Association; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; ICM, ischemic cardiomyopathy; IQR, interquartile range; LAE, left atrial enlargement; ↑LVWT, increased left ventricular wall thickness; TIA, transient ischemic attack; VHD, valvular heart disease

and prior stroke/transient ischemic attack history. CB done as a redo procedure was equally common in the studied groups (Table 1).

Table S1 presents a comparison of the drug therapy used in the studied groups. Overall, 185 (74%) patients were receiving Vaughan Williams class I/III antiarrhythmic agents in the hospital or at discharge, with an overall similar frequency across the studied groups but more frequent amiodarone use among subjects in the increased LVWT (+)LAE(+) group. Statins were used more often among subjects with increased LVWT, whereas patients with LAE were more often treated with vitamin K antagonists.

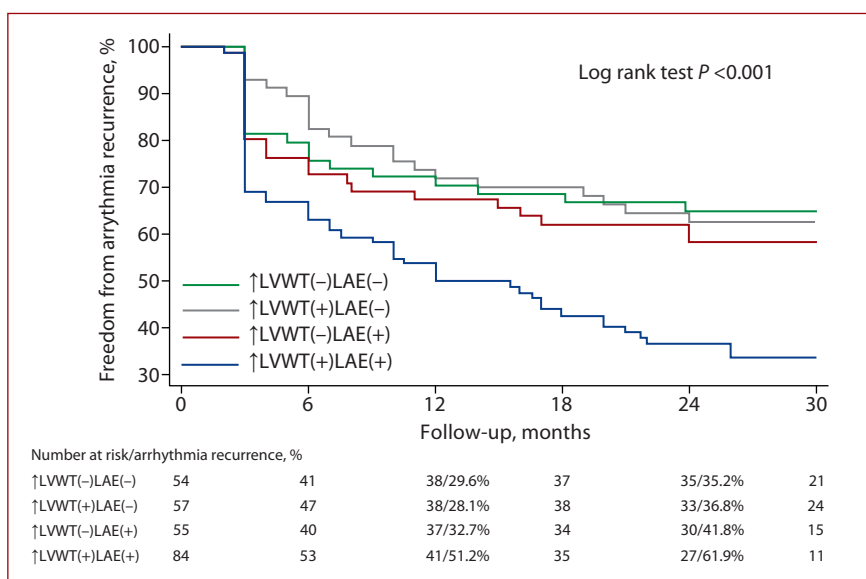
Table S2 presents a comparison of baseline anatomy assessed using 2D-echo or MSCT among the studied groups. Common/accessory PVs were identified with similar frequency across the groups, but more frequently using MSCT than transesophageal echocardiography (TEE) (41.6% vs. 11.7%; P < 0.001, respectively).

Table S3 presents a comparison of the procedural parameters among the studied groups. Patients with either LAE or increased LVWT were treated with bigger balloons (28 mm). Overall, LA dwell time and the number of freezing applications and their duration were all similar in the studied groups and did not differ between groups with vs. without common/accessory PVs. Patients with LAE had longer fluoroscopy time (20.0 [14.4–24.5] vs. 17.2 [12.0–23.0] minutes in subjects without LAE, P = 0.027).

### Short and long-term outcomes

Median follow-up was 24.5 (IQR, 6.0–31.00) months, with 100% of patients who achieved 2-year follow-up with no deaths. There was only one serious potentially procedure-related adverse event (stroke) — it manifested early (within hours) post-procedure, was documented by magnetic resonance as a single acute ischemic lesion, and occurred despite the fact that the patient had been on warfarin up to the ablation procedure and the TEE index excluded LA thrombus. There were no other major complications such as major bleeding (with blood transfusion), cardiac tamponade, phrenic nerve palsy, esophageal perforation/fistula, or death. Overall, 34.1% (63/185) of patients with antiarrhythmic drugs (class I/III) at discharge had the drugs subsequently discontinued (Supplementary material, Table S1), but this was less frequent among patients from the increased LVWT (+)LAE(+) group.

Despite overall arrhythmia recurrence rates of 37.2% (n = 93) at 1-year and 46.0% (n = 115) at 2-year follow-up, significant improvement in arrhythmia-related symptoms was noticed in 38.3% of these (P < 0.001). The highest rate of 2-year arrhythmia recurrence was encountered in the increased LVWT (+)LAE(+) group (61.9%); the intermediate rate — among subjects with isolated LAE (41.8%); and the lowest — among patients with isolated increased LVWT or increased LVWT (-)LAE(-) (36.8% and 35.2%, respectively; Figure 1; P = 0.004). Long-term outcomes were similar



**Figure 1.** Kaplan-Meier curves of freedom from arrhythmia recurrence for the studied groups (100% of patients accomplished 2-year follow-up)

Abbreviations: ↑LVWT, increased left ventricular wall thickness; LAE, left atrial enlargement

**Table 2.** Predictors of arrhythmia recurrence

	Univariate			Multivariable		
	HR	95% CI	P-value	HR	95% CI	P-value
BMI	1.039	0.985–1.096	0.164	1.014	0.959–1.071	0.63
Paroxysmal AF	0.517	0.360–0.741	<0.001	0.593	0.401–0.877	0.009
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	1.134	0.999–1.288	0.052	1.083	0.951–1.233	0.23
VHD	1.930	0.977–3.811	0.058	1.480	0.735–2.980	0.27
CM	0.918	0.578–1.458	0.717	0.747	0.461–1.210	0.24
↑LVWT(+)-LAE(-) <sup>a</sup>	1.037	0.557–1.929	0.909	0.947	0.507–1.770	0.87
↑LVWT(-)-LAE(+) <sup>a</sup>	1.282	0.702–2.340	0.419	1.062	0.570–1.977	0.85
↑LVWT(+)-LAE(+) <sup>a</sup>	2.268	1.344–3.828	0.002	1.784	1.017–3.130	0.04

<sup>a</sup>Versus the risk of the reference group: ↑LVWT(-)-LAE(-)

Abbreviations: CI, confidence interval; HR, hazard ratio; other — see Table 1

between the groups with vs. without common/accessory PV (correspondingly arrhythmia recurrence at 2 years of 48.8% vs. 44.5%;  $P = 0.59$ ).

Both LAE and increased LVWT raise the risk of arrhythmia recurrence (HR, 1.801; 95% CI, 1.230–2.636;  $P = 0.002$  and HR 1.495; 95% CI, 1.028–2.175;  $P = 0.04$ , respectively). There was no evidence of difference in the predictive value of LAE defined by MSCT (HR, 1.842; 95% CI, 1.195–2.838;  $P = 0.006$ ) and 2D-echo (HR, 1.659; 95% CI, 0.734–3.748;  $P = 0.22$ ) ( $P$ -value for interaction = 0.74). Paroxysmal AF was associated with a lower rate of arrhythmia recurrence (29.1% at 1 year and 37.1% at 2 years vs. 49.5% and 59.6% in other patients, both  $P = 0.001$ ). There was a trend for a higher CHA<sub>2</sub>DS<sub>2</sub>-VASc score and more frequent VHD among patients with arrhythmia recurrence ( $P = 0.09$  and  $P = 0.07$ ). CB ablation was similarly effective in patients with the first or redo procedure (44.5% vs. 50% of arrhythmia recurrence at 2 years;  $P = 0.48$ , respectively).

After adjustment for BMI, paroxysmal AF, CHA<sub>2</sub>DS<sub>2</sub>-VASc score, VHD, and CM, patients with LAE and concomitant increased LVWT had a 1.8-times increased risk of arrhythmia recurrence, whereas, with paroxysmal AF, the risk was 1.7-times lower (Table 2).

## DISCUSSION

This is the first study to report the prognostic importance of concomitant increased LVWT and LAE on arrhythmia recurrence in patients treated with CB for AF, regardless of whether it is the first or a redo procedure. The main findings were as follows: (1) CB procedural safety was excellent, with only one serious potentially procedure-related adverse event; (2) whereas the overall 1-year and 2-year arrhythmia recurrence were 37.2% and 46.0%, respectively, substantial (38.3%) improvement in arrhythmia-related symptoms and EHRA was noted among subjects with subsequent arrhythmia; (3) even though increased LVWT without LAE was not



associated with a higher risk of arrhythmia recurrence, joint diagnosis of LAE and increased LVWT was associated with the highest arrhythmia recurrence: 51.2% at 1 year and 61.9% at 2 years, with paroxysmal AF being an independent predictor of a lower risk of arrhythmia recurrence; (4) neither common/accessory PV nor a redo procedure was associated with arrhythmia recurrence; (5) there was no evidence of a difference in the predictive value of LAE defined by MSCT vs. 2D-echo; it might warrant future studies to compare the predictive performance of these in terms of baseline LV remodeling assessment.

The procedural safety of CB in our experience is in line with large-scale real-life observational studies [18]. In our study, there was only one serious potentially procedure-related adverse event — stroke — manifesting early (within hours) post-procedure, which occurred despite anticoagulation and exclusion of LA thrombus by TEE index. It was the only stroke in the 2016–2021 period, during which 912 AF ablations were performed. Recent studies suggested a role of gas emboli, but not clot formation, in the pathophysiology of ischemic brain lesions associated with a CB procedure. Thus, procedural factors should be taken into consideration to lower ischemic lesions risks [19].

In a large German study of 605 patients treated with CB for AF, arrhythmia recurrence at >12 months was 38%, lower than the current 46% rate at 2 years (our 1-year rate was 37.2%); however, the percentage of paroxysmal AF patients was 96% in the German study and only 60% in our study. Importantly, in the current analysis, paroxysmal AF appears to be the strongest predictor of favorable long-term outcomes. Substantial differences in  $\text{CHA}_2\text{DS}_2\text{-VASc}$  and frequency of arterial hypertension were also noted between the German patients' group and our cohort (0.7 vs. 2.0 and 42% vs. 68%, respectively) [20]. Furthermore, in almost a third of current cases, CB was a redo ablation, and 17.6% of our subjects had long-persistent AF, typically excluded in most of the published studies [20–22]. In large prospective studies, significant improvement in the quality of life after AF ablation is reported on average in 42%–56% and even up to 76% of patients with arrhythmia recurrence at 12 months, which is similar to the current results [22, 23]. In our study among patients with arrhythmia recurrence, significant EHRA reduction was noticed in follow-up,  $P < 0.001$ ; in consequence, only 36% of patients with arrhythmia recurrence (42/115) were qualified for re-ablation.

Our findings were in line with the broad literature indicating that major predictors of arrhythmia recurrence after CB were non-paroxysmal AF and LAE [2, 4, 24]. Both factors were associated with more advanced atrial cardiomyopathy, suggesting its main role in arrhythmia recurrence [25]. Only the joint diagnosis of LAE and increased LVWT was associated with a significantly elevated arrhythmia recurrence rate, and not isolated increased LVWT. The effect of increased LVWT might be mediated by its association with more advanced atrial remodeling in the setting of LAE. Notably, indexed LA volumes measured with MSCT

in the current study were bigger than those assessed with 2D-echo, with an average difference of 9.0 (3.5)  $\text{cm}^3/\text{m}^2$  being similar to the extent of LA volume underestimation reported for 2D-echo vs. cardiac magnetic resonance [26].

Our results might indicate that echocardiography identifies common/accessory PVs less frequently than MSCT despite an overall 34.4% frequency of patients with common/accessory PVs in our study, similar to a reported 39.7% rate in the other studies [27, 28]. Contrary to a previous study suggesting an association of accessory PVs with a higher recurrence rate after CB for AF, we did not find such a relationship [29]. The previous study [27] documenting such a relationship created a composite score defining an “unfavorable” LA-PV anatomy, with detailed evaluation of the LA cavity and PV antral anatomies (including dimensions, eccentricity indexes, and angles) in addition to the presence of an accessory PV. Patients with an “unfavorable” LA-PV anatomy, identified using the above score, required longer cryoablation, similar to our results documenting longer fluoroscopy times among patients with LAE. Since we did not find a predictive value of an accessory PV, our results supported the notion that it was actually LA dimensions and not “unfavorable” LA-PV anatomy that predicted arrhythmia recurrence, similar to a previously published study [30].

Only advanced imaging modalities (cardiovascular magnetic resonance/angio-computed tomography) can precisely evaluate the LA cavity, structure, and its function (strain and ejection fraction); all provide novel metrics that might possess additional prognostic value (e.g. posterior left atrial adipose tissue attenuation as a promising predictor of arrhythmia recurrence after catheter ablation) [31, 32]. Our findings are in line with current knowledge of the potential impact of various LAE etiologies, with a frequent LAE finding in patients with preserved systolic LV function, but hypertrophic LV and its diastolic dysfunction [33].

### Limitations

This was a single-center retrospective study. The follow-up was partly conducted during the COVID-19 pandemic. The use of regular 7-day Holter monitoring or implantable continuous loop recorders would make it possible to determine the type of arrhythmia recurrence and its burden and thus an accurate recurrence rate (the current one might be overestimated). This is particularly relevant for subjects treated for persistent and long-persistent AF in whom the therapeutic target relies more on significant arrhythmic burden reduction rather than on its total elimination. More profound insights into LV remodeling stratified according to its relative wall thickness and mass would have allowed for a better understanding of different LAE etiologies [34, 35].

### CONCLUSIONS

Joint diagnosis of increased LVWT and LAE increases substantially the risk of arrhythmia recurrence after cry-

oballoon ablation for AF. The simplest echocardiographic measure of LVWT adds substantial prognostic information allowing for a reliable, easy, fast, and early risk stratification. Prevention and accurate treatment of arterial hypertension, the major cause of increased LVWT and thus left atrial myopathy [36], is of particular importance among patients with AF scheduled for CB procedures.

### Article information

**Conflict of interest:** MS — investigational, consulting, and lecturer's fees from Abbott, Biotronik, and Medtronic. Other authors have no conflicts of interest with regard to this manuscript.

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