Cardiac Computed Tomography-Derived Left Atrial Volume Index as a Predictor of Long-Term Success of Cryo-Ablation in Patients With Atrial Fibrillation

Julian Maier, MD[a,b,#,*], Hermann Blessberger, MD[a,#], Alexander Nahler, MD[a], Denis Hrncic, MD[a], Alexander Fellner, MD[a], Christian Reiter, MD[a], Simon Hönig, MD[a], Pierre Schmit, MD[c], Franz Fellner, MD[c], Thomas Lambert, MD[a], and Clemens Steinwender, MD[a]

Patients with symptomatic, drug-refractory atrial fibrillation (AF) are frequently treated with catheter ablation. Cryo-ablation has been established as an alternative to radiofrequency ablation but long-term outcome data are still limited. This study aimed at elucidating the influence of the left atrial volume index (LAVI), derived from cardiac computed tomography (cCT) data, on the long-term outcome of ablation-naïve AF patients, after their first cryo-ablation. 415 patients (n = 290 [69.90%] male, 60.00 [IQR: 53.00 to 68.00] years old) who underwent a cCT and subsequent cryo-ablation index procedure were included in this single centre retrospective data analysis. A composite end point was defined (AF on electrocardiogram and/or electric cardioversion and/or re-do). Patients were closely followed for a year and then contacted for long-term follow-up after a median of 53.00 months (IQR: 34.50 to 73.00). Statistical analyses of the outcome and predictors of AF recurrence were conducted. In 224 patients (53.98%) no evidence of AF recurrence could be found. LAVI differed significantly between the positive and adverse (AF recurrence) outcome group (49.96 vs 56.07 ml/m^2, $p < 0.001$). Cox regression analyses revealed cCT LAVI (HR: 1.022, 95% CI: 1.013 to 1.031, $p < 0.001$), BMI (HR: 1.044, 95% CI: 1.005 to 1.084, $p < 0.05$) and the type of AF (HR: 1.838 for nonparoxysmal AF, 95% CI: 1.214 to 2.781, $p < 0.01$) to be effective predictors of AF recurrence. A prognostic cCT LAVI cut-off value of 51.99 ml/m^2 was calculated and must be validated in future prospective studies. In conclusion, LAVI is an accurate, yet underutilized predictor of AF recurrence after pulmonary vein isolation with cryo-energy and scores for calculating AF recurrence or progression risks might underemphasize the importance of CT-derived LAVI as a predictive factor. **(Am J Cardiol 2021;140:69−77)**

Atrial fibrillation (AF) is the most common arrhythmia in the adult population, with its prevalence continuously rising.[1] It is associated with significant morbidity and mortality, leading to pronounced socio-economic effects.[2] Catheter ablation, and more specifically pulmonary vein isolation (PVI), is the recommended treatment for patients suffering from drug-refractory, symptomatic paroxysmal, or persistent AF.[3,4] During the last decade, cryo-ablation has been established as an alternative to traditional radiofrequency (RF) ablation and recent studies emphasize the comparability of the outcome of the 2 methods.[5-7] Advantages of cryo-balloon ablations are the shorter duration of the procedure, less pronounced side-effects with the exception of an increase in transient phrenic nerve palsy, and the potentially better reproducibility.[8,9] This study is one of the still few studies on the long-term success of cryo-ablation index procedures in ablation-naïve AF patients. Furthermore, 1 major factor, left atrial volume at the time of the procedure, was evaluated as a predictor of cryo-ablation success.

Methods

Five hundred patients suffering from paroxysmal or nonparoxysmal AF[3] who underwent their first PVI by cryo-balloon ablation at the Kepler University Hospital in Linz, Austria, between 2009 and 2017 comprise the patient population of this study. Patients who received RF ablations or re-do cryo-ablations were excluded. Patients with critical data (such as CT measurements) missing, were omitted from the analysis (see Appendix A for a study flowchart). Thus, data from 415 patients were anonymized and included in the statistical analysis. The study conforms to current ethical guidelines and was approved by the local ethics committee.

The primary end point of the study was the recurrence of AF. This was operationalized as a composite end point that was defined as follows: When (1) an instance of AF was

[a]Department of Cardiology, Kepler University Hospital, Medical Faculty, Johannes Kepler University Linz, Linz, Austria; [b]Institute of Pharmacology, Center for Physiology and Pharmacology, Medical University of Vienna, Vienna, Austria; and [c]Central Radiology Institute, Kepler University Hospital, Medical Faculty, Johannes Kepler University Linz, Linz, Austria. Manuscript received August 29, 2020; revised manuscript received and accepted October 27, 2020.

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#contributed equally

*Corresponding author: Tel: +43 (0)5 7680 83 − 6220; fax: +43 (0)5 7680 83 - 6205.

E-mail address: julian.maier@meduniwien.ac.at (J. Maier).

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detected on an electrocardiogram (ECG-at least 30 seconds in duration) and/or (2) an electric cardioversion due to AF recurrence and/or (3) a re-do of the procedure due to AF recurrence were necessary, the outcome was deemed adverse. The first 3 months of postablation tissue healing were considered as a blanking period during which the primary end point could not be reached.

All patients underwent cardiac computed tomography (cCT) before the procedure to assess pulmonary vein anatomy. cCT imaging was performed with a Dual Source (2×192 slice) CT (Somatom Force, Siemens, Erlangen, Germany). Acquisition was ECG gated with dose modulation and conducted during an end-inspiratory breath hold after a body weight adapted bolus injection of iodide contrast medium (Iomeron 400 mg J/ml, Bracco imaging S.p.A., Milan, Italy). Parameters utilized were: 0.6 mm beam collimation, 0.6 mm thickness, 0.4 mm increment, and 20 to 30 cm field of view. cCT imaging raw data was imported in the segmentation software EnSite Verismo (Abbott, North Chicago, Illinois). After inputting the borders of the left atrium and multiplanar segmentation, contours of the left atrium were automatically drawn and manually adjusted by referencing a reconstructed 3-D model (see Appendix B). Measurements were taken during left-ventricular systole. Left atrial volume was calculated after the exclusion of the pulmonary veins (PV). The image analysis was conducted by an experienced observer, blinded to patient- and outcome-specific data.

For cryo-balloon catheter ablations, patients were deeply sedated with midazolam, propofol (2%) and fractionated fentanyl. Diagnostic catheters were placed in the coronary sinus and in the His region. The latter was used as a marker during transseptal puncture and, after repositioning, to stimulate the phrenic nerve during cryo-ablation of the right superior and inferior PV. After entry through the right femoral vein, the left atrium was accessed through transseptal puncture, aided by pressure monitoring and fluoroscopy. An oesophageal probe was used for continuous temperature monitoring. The cryo-balloon ablation system (first generation Arctic Front or second generation Arctic Front Advance, Medtronic Inc., Minneapolis, Minnesota) with either a 23 or a 28 mm balloon, was inserted through a steerable sheath (FlexCath [Advance] 15 Fr sheath, Medtronic Inc.). An Achieve mapping catheter (Medtronic Inc.) was applied for the recording of PV signals. PVs were located by selective pulmonary vein angiography with the FlexCath sheath. The cryo-balloon was inflated at the antrum of the PVs and then advanced forward until occlusion of the vein, which was confirmed by contrast agent injection during fluoroscopy. Cryo-energy delivery was immediately stopped when phrenic nerve function appeared to be impaired, as assessed by haptic manual feedback of diaphragmic movement. For each PV, 1-2 ablation cycles were performed, depending on the time to isolation and obtained freeze temperature. In case of nonsatisfactory results, a maximum of 5 freezes was allowed. Success of cryo-ablation was confirmed by entry and exit block after 30 minutes or testing for spontaneous reconnections under bolus administration of adenosine. Vital parameters (ECG, blood pressure, and oxygen saturation) were constantly monitored. All ablations were conducted by 1 of 3 experienced interventionalists.

After discharge, outpatient check-ups at our clinic were scheduled for patients at 3 and 12 months post intervention. A routine Holter ECG and resting ECG was performed after 3 and 12 months, respectively. Additional resting ECGs, event recorders or 24-hrs Holter ECGs were utilised to verify AF recurrence in case of symptoms typical of AF. Patients were encouraged to contact the clinic anytime they noticed symptoms, in which case a check-up was scheduled as soon as possible. Additionally, office-based cardiologists and general practitioners referred patients with confirmed or assumed AF recurrence back to our department.

Between 2018 and 2019, all patients were contacted through telephone and interviewed about possible AF relapses, cardioversions or ablation procedures. Patients reported whether they had a documented recurrence of AF, received an electric cardioversion or ablation procedure (at another institution) after the index procedure at our hospital. In the case of an affirmative answer, we requested discharge letters and results from diagnostic procedures to assess whether the primary end point had been met. If necessary, such as in the case of mentioned symptoms suggesting AF recurrence, check-ups at our clinic were scheduled. If patients could not be reached by phone, letters with the request to contact the study team were mailed to their home addresses. If no contact could be established, the Austrian resident register was consulted to identify new contact information. If patients chose not to participate in the follow-up interview, they were excluded from the investigation.

Categorical variables are presented as percentages and frequencies and compared with Pearson's chi-square test. The normality of the distribution of the variables was assessed with the Kolmogorov-Smirnov and Shapiro-Wilk test. Continuous variables are given as mean values (±SD), when normally distributed, or medians (with Interquartile range) and compared by making use of Student's *t* test for normally distributed variables or the nonparametric Mann-Whitney *U*-test. The continuous variable left atrial volume index (LAVI) was grouped into terciles. Subsequently, Kaplan-Meier curves were plotted and the log-rank test performed to test for differences in AF recurrence between groups. Cox regression analyses were conducted to adjust for covariates and potential confounders (age; antiarrhythmic drug use; body mass index; cerebrovascular accident; coronary artery disease; diabetes mellitus; glomerular filtration rate; left ventricular ejection fraction; mean arterial pressure; sex). The proportional hazards assumption was confirmed for each variable with Schoenfeld residuals. For a future prospective study, a prognostic LAVI cut-off value was determined by plotting a receiver operating characteristic (ROC) curve and calculating the Youden index (sensitivity+specifity-1), with the maximum value, combining the highest specificity and sensitivity, serving as the optimal cut-off point. All statistical analyses were performed using R Studio version 1.2.5001 (R Studio Inc., Boston, Massachusetts) and SPSS Statistics version 25.0 (IBM, Armonk, New York). A p-value <0.05 was considered statistically significant.

Results

The median amount of time between PVI and follow-up was 53.00 months (Interquartile range: 34.50 to 73.00). The 415 patients included in the study were divided into 2 groups, based on the long-term outcome after their first ablation procedure. In 224 patients (53.98%) we found no evidence of AF recurrence (positive outcome), whereas 191 patients (46.02%) met the composite primary end point (adverse outcome). Table 1 indicates that the 2 groups are relatively homogenous concerning baseline characteristics, including preexisting conditions and medication taken pre-intervention. Most patients were male (69.90%), around 60.00 (53.00 to 68.00) years old and overweight (BMI = 27.27 ± 4.09) at the time of the procedure.

The frequency of the type of AF differed significantly between the groups, with more patients with nonparoxysmal AF suffering from AF recurrence. In addition, the EHRA score of pre-intervention symptom severity, was higher in the adverse outcome group.

Even though very few AF patients of this cohort (2.89%) suffered from valvular heart disease, their share varied significantly between the 2 groups. Patients suffering from moderate or severe aortic or tricuspid regurgitation were present in both groups, whereas mitral regurgitation was associated with an AF relapse (these patients had more adverse outcomes [$p = 0.016$] and a significantly larger LAVI than the other patients [$p < 0.001$]).

Marked differences between the 2 groups could be found in the measurement of left atrial volumes (LAV) and the calculation of LAVI of the patients. The median LAV of the positive outcome group was 97.00 ml (83.25 to 117.00), with a LAVI of 49.96 ml/m^2 (42.05 to 59.00) and the adverse outcome group had a median LAV of 114.00 ml (96.00 to 137.00), with a LAVI of 56.07 ml/m^2 (48.45 to 69.66). The differences between the groups were highly significant ($p < 0.001$, respectively). See Figure 1 for the distribution of the variable LAVI.

The duration of the ablation procedures was on average 90 minutes with a total freeze time of 19 minutes. For the adverse outcome group, the duration and freeze time were slightly longer, although not reaching statistical significance. Most procedures were deemed successful with complete PV isolation in 398 of the cases (95.90%). Complications included transient phrenic nerve palsy (10.36%) and pericardial effusion not requiring pericardiocentesis (5.78%) as the most common ones. Concerning the cases of transient nerve palsy, the complication subsided in all patients during the first year after the procedure. For an overview of procedural data and periprocedural complications see Table 2.

Patients were grouped into terciles based on their LAVI (first tercile cut-off: 47.28 ml/m^2, second cut-off value: 58.80 ml/m^2). A Kaplan-Meier curve, showing the cumulative freedom of AF recurrence for the terciles over time, is depicted in Figure 2. The log-rank test revealed that the differences between terciles were highly significant ($p < 0.0001$).

In univariate Cox regression analyses, lower EF, suffering from nonparoxysmal AF, a higher LAVI, and belonging to a higher LAVI tercile were shown to be significant

Table 1
Clinical characteristics of the study population, divided into two groups according to outcome and compared statistically

Variable	All (n = 415)	Positive outcome (n = 224, 53.98%)	Adverse outcome (n = 191, 46.02%)	p-value
Men	290 (69.90%)	163 (72.80%)	127 (66.50%)	0.165
Age (years)	60.00 (53.00−68.00)	59.00 (53.00−67.00)	61.00 (53.00−69.00)	0.098
BMI (kg/m^2)	27.27 ± 4.09	27.02 ± 3.84	27.56 ± 4.36	0.175
Atrial fibrillation type				
Nonparoxysmal	47 (11.33%)	16 (7.14%)	31 (16.23%)	0.004
Paroxysmal	368 (88.67%)	208 (92.86%)	160 (83.77%)	0.004
EHRA score (1-4)				
Pre-intervention	3.35 ± 0.80	3.25 ± 0.85	3.47 ± 0.72	0.031
Preexisting conditions				
Coronary artery disease	45 (10.84%)	20 (8.93%)	25 (13.09%)	0.174
Peripheral artery disease	6 (1.45%)	2 (0.89%)	4 (2.09%)	0.307
Cerebrovascular accident	18 (4.34%)	11 (4.91%)	7 (3.67%)	0.424
Diabetes mellitus	32 (7.71%)	17 (7.59%)	15 (7.85%)	0.920
Hypercholesterolemia	279 (67.23%)	157 (70.09%)	122 (63.87%)	0.179
Hypertension	222 (53.49%)	114 (50.89%)	108 (56.54%)	0.250
Valvular heart disease	12 (2.89%)	3 (1.34%)	9 (4.71%)	0.041
Medication (pre-intervention)				
β-blocker	205 (49.40%)	103 (45.98%)	102 (53.40%)	0.132
Antiarrhythmic	136 (32.77%)	67 (29.91%)	69 (36.13%)	0.179
Sotalol	62 (14.94%)	33 (14.73%)	29 (15.18%)	0.898
DOAC	147 (35.42%)	78 (34.82%)	69 (36.13%)	0.782
Vitamin K antagonist	240 (58.83%)	133 (59.38%)	107 (56.02%)	0.490
Other anticoagulants/combination	28 (6.75%)	13 (5.80%)	15 (7.85%)	0.407
Physiological measurements				
Left atrial volume (cc)	106.00 (87.00−129.00)	97.00 (83.25−117.00)	114.00 (96.00−137.00)	<0.001
Left atrial volume index (ml/m^2)	52.46 (44.12−63.22)	49.96 (42.05−59.00)	56.07 (48.45−69.66)	<0.001
Left ventricular ejection fraction (%)	62.08 ± 5.52	62.64 ± 4.99	61.45 ± 6.01	0.058
Mean arterial pressure (mm Hg)	102.50 (95.00−110.00)	102.50 (95.00−110.00)	102.50 (95.00−110.00)	0.890

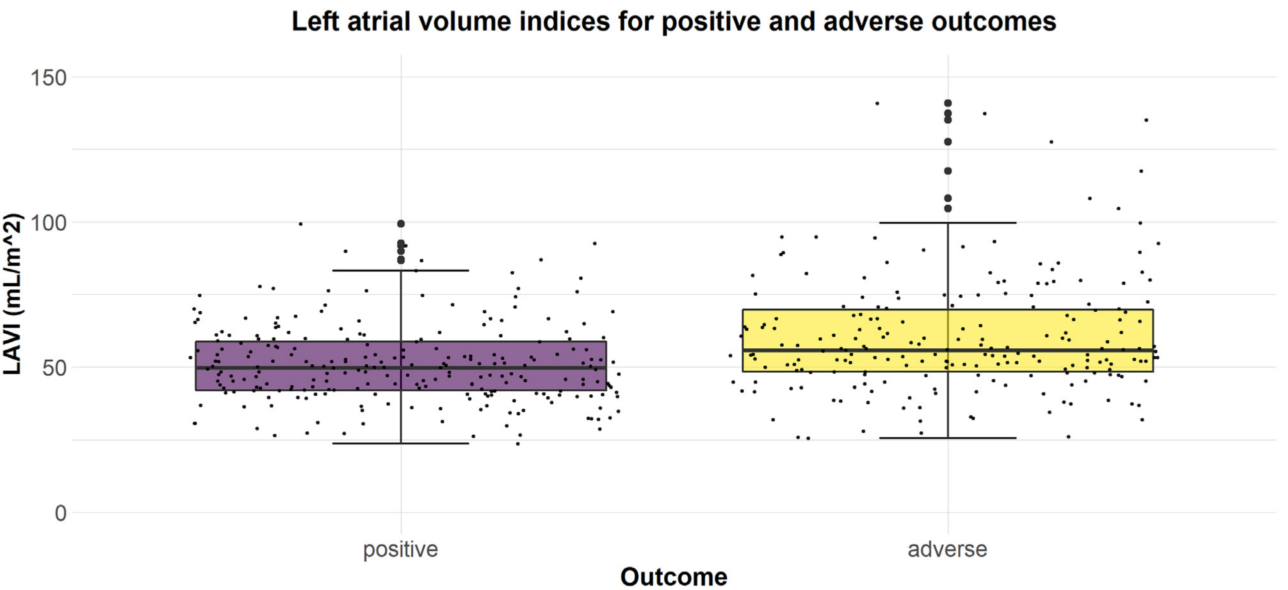

Figure 1. Jitter scatter-/boxplot, showing patient LAVI values (ml/m^2, small black dots) and the boxplots for the positive and adverse outcome groups. LAVI: left atrial volume index.

predictors of early AF recurrence. In addition, higher age and BMI, as well as female gender were identified as risk factors bordering significance. For an overview, see Table 3A.

Cox multiple regression analyses confirmed that LAVI grouped into terciles and indexed LAV were in the strongest predictors of AF recurrence in their respective models (see Tables 3B and 3C). The hazard ratio (HR) of LAVI terciles 2 and 3, when compared with reference tercile 1 was 1.604 (95% CI: 1.05 to 2.450) and 2.157 (95% CI: 1.400 to 3.324) respectively, whereas the HR for LAVI was 1.022 (95% CI: 1.013 to 1.031). Additional relevant predictors of adverse outcomes were nonparoxysmal AF (HR model 1: 1.907 [95% CI 1.284 to 2.833]; HR model 2: 1.838 [95% CI: 1.214 to 2.781]) and a higher BMI (in model 1, HR: 1.042, 95% CI: 1.004 to 1.082; in model 2, HR: 1.044, 95% CI: 1.005 to 1.084), with the factor female sex being close to the threshold of significance. For a Kaplan-Meier curve with patients grouped according to the type of AF, see Appendix C.

Although grouping patients into terciles according to their LAVI is a reasonable approach to stratify individual risk, an alternative would be to establish an optimal, prognostic LAVI cut-off value. For this purpose, a receiver

Table 2
Procedural data and periprocedural complications, divided into two groups according to outcome and compared statistically

Variable	All (n = 415)	Positive outcome (n = 224, 53.98%)	Adverse outcome (n = 191, 46.02%)	p-value
Procedure				
Duration (min)	90.00 (70.00−130.00)	90.00 (70.00−120.00)	95.00 (70.00−135.00)	0.097
Total freeze time (min)	19.00 (16.00−25.00)	19.00 (16.00−25.00)	20.00 (16.00−26.00)	0.159
Fluoroscopy time (min)	19.00 (12.00−28.00)	18.00 (12.00−26.75)	20.00 (13.00−30.00)	0.097
Common ostium	7 (1.69%)	4 (1.79%)	3 (1.57%)	0.865
Pulmonary veins	7 (1.69%)	4 (1.79%)	3 (1.57%)	0.244
3	379 (91.32%)	200 (89.29%)	179 (93.72%)	0.701
4	29 (6.99%)	20 (8.93%)	9 (4.71%)	
5	398 (95.90%)	214 (95.54%)	184 (96.34%)	
Complete pulmonary vein isolation				
Complications				
Vagal reaction	9 (2.17%)	4 (1.79%)	5 (2.62%)	0.562
Transient phrenic nerve palsy (<=1 year)	43 (10.36%)	22 (9.82%)	21 (10.99%)	0.696
Permanent phrenic nerve palsy (>1 year)	0	0	0	-
Pericarditis	3 (0.72%)	0	3 (1.57%)	0.060
Pericardial effusion	27 (6.50%)	14 (6.25%)	13 (6.81%)	0.819
Requiring pericardiocentesis	3 (0.72%)	1 (0.45%)	2 (1.05%)	0.462
Pneumothorax	1 (0.24%)	1 (0.45%)	0	0.355
Arteriovenous fistula	2 (0.48%)	0	2 (1.05%)	0.265
Cerebrovascular accident	4 (0.96%)	2 (0.89%)	2 (1.05%)	0.873
Oesophageal fistula	0	0	0	-
Death	0	0	0	-

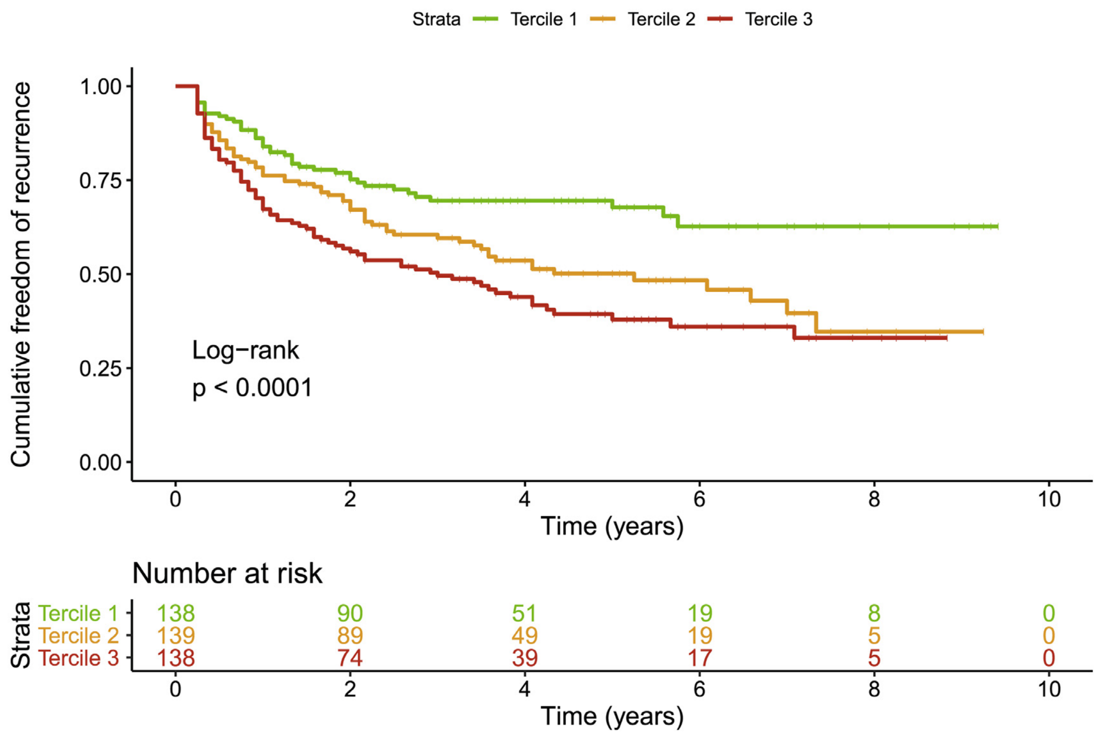

Figure 2. Kaplan-Meier curves with accompanying risk table of the 3 LAVI terciles and their freedom of recurrence over time. LAVI: left atrial volume index.

operating characteristic (ROC) curve was plotted (AUC: 0.647, 95% CI: 0.594 to 0.700, p-value < 0.001-null hypothesis: no difference from AUC = 0.5) and the maximal LAVI Youden index value (51.99 ml/m^2) determined (see Figure 3A). Although the derived cut-off value is to be confirmed in future prospective studies, to illustrate its appropriateness for the herein analysed patient population, a Kaplan-Meier curve, utilizing the calculated cut-off value to distinguish between the 2 LAVI groups, can be appreciated in Figure 3B.

For the purpose of comparing this study's data with previous studies that did not use LAVI as a parameter, the same analysis was conducted with left atrial volume, yielding a maximal Youden index value of 98.50 ml (see Appendix D).

Discussion

This study is one of the still few to provide extended long-term outcome data of cryo-ablation index procedures in ablation-naïve patients with a median follow-up of 53 months. LAVI was identified as a highly relevant predictor of AF recurrence and an optimal cut-off value was calculated, enabling the stratification of patients according to their risk of recurrence in future prospective studies and in clinical practice.

Two hundred and twenty-four of the 415 treated patients remained free from AF recurrence (53.98%). Although several studies have reported short- and mid-term (<1 year) follow-up data,[10] long-term follow-up studies for cryo-ablation are still scarce.[6,11−14] Nevertheless, the existing long-term outcome studies for RF and cryo-ablation show similar success rates as the current study, mostly between 50 and 60% after the index procedure,[15,16] with various trials emphasizing the comparability of RF and cryo-ablation outcome data.[5,6] This study's results solidify the proposed similarity in long-term outcomes between RF and cryo-ablation index procedures.

A previously reported[10] high incidence of transient phrenic nerve palsy, common to cryoballoon ablation, was also observed in this patient cohort. The rate of pericardial effusion incidents was an additional, known, relatively frequent complication reported herein.[10]

Serious complications such as cardiac tamponade, CVA, oesophageal fistula or death could be corroborated to be very rare, making cryo-balloon ablation a safe interventional strategy for AF management.

Although previous studies' identification of predictive factors has been quite heterogenous, many have identified nonparoxysmal AF as the essential determinant of the outcome.[17] This study could corroborate that nonparoxysmal AF is an important factor in predicting AF recurrence. Still, with the small sample size of patients with nonparoxysmal AF in this cohort (n = 47, 11.33%), further statistical comparisons with the large group of paroxysmal AF patients (n = 368, 88.67%) do not appear to be meaningful.

In addition, we found a higher BMI to be a significant predictive factor of adverse outcomes. Gender, age, hypertension, CAD, diabetes mellitus, and EF (amongst others) could not be identified as prognostic factors, which was also the case in previous studies.[17] Although this study only had 6 patients with moderate mitral regurgitation, all had adverse outcomes and a significantly larger LAVI than the rest of the cohort. It has been shown before that mitral

Table 3
(A) Univariate cox regression analysis, (B) Cox multiple regression model 1, (C) Cox multiple regression model 2, indicating the influence of left atrial volume index and other variables on the outcome

A) Univariate Cox regression	Unadjusted HR	95% CI	p-value
Cerebrovascular accident	1.258	0.591−2.677	0.552
Coronary artery disease	0.803	0.527−1.222	0.306
Mean arterial pressure (mm Hg)	0.998	0.987−1.009	0.732
Left ventricular ejection fraction (%)	0.974	0.952-0.997	0.025
Glomerular filtration rate (ml/min)	0.999	0.991−1.006	0.746
Female sex	1.339	0.991−1.809	0.057
Age (years)	1.013	0.999−1.028	0.065
BMI (kg/m^2)	1.035	0.999−1.072	0.056
Diabetes mellitus	1.041	0.614−1.765	0.881
Antiarrhythmic drug treatment	0.783	0.582−1.053	0.105
Nonparoxysmal atrial fibrillation	1.992	1.353−2.933	<0.001
Left atrial volume index (ml/m^2)	1.023	1.015−1.031	<0.001
Left atrial volume index terciles	1.468	1.228−1.756	<0.001
B) Cox multiple regression model 1 (LAVI terciles)	**Adjusted HR**	**95% CI**	**p-value**
Cerebrovascular accident	0.562	0.255−1.240	0.154
Coronary artery disease	1.310	0.826−2.078	0.251
Mean arterial pressure (mm Hg)	0.992	0.980−1.004	0.181
Left ventricular ejection fraction (%)	0.989	0.964−1.014	0.379
Glomerular filtration rate (ml/min)	1.004	0.995−1.013	0.359
Female sex	1.164	0.987−1.373	0.072
Age (years)	1.008	0.988−1.027	0.444
BMI (kg/m^2)	1.042	1.004−1.082	0.028
Diabetes mellitus	0.733	0.400−1.343	0.315
Antiarrhythmic drug treatment	1.253	0.916−1.712	0.158
Non-paroxysmal atrial fibrillation	1.907	1.284−2.833	0.001
Left atrial volume index tercile 1 (reference)			0.002
Left atrial volume index tercile 2	1.604	1.051−2.450	0.029
Left atrial volume index tercile 3	2.157	1.400−3.324	<0.001
C) Cox multiple regression model 2 (LAVI)	**Adjusted HR**	**95% CI**	**p-value**
Cerebrovascular accident	1.860	0.837−4.133	0.128
Coronary artery disease	0.834	0.520−1.337	0.451
Mean arterial pressure (mm Hg)	0.992	0.979−1.004	0.186
Left ventricular ejection fraction (%)	0.993	0.968−1.019	0.598
Glomerular filtration rate (ml/min)	1.003	0.994−1.012	0.539
Female sex	1.343	0.531−1.043	0.086
Age (years)	1.005	0.985−1.024	0.648
BMI (kg/m^2)	1.044	1.005−1.084	0.026
Diabetes mellitus	1.185	0.643−2.181	0.586
Antiarrhythmic drug treatment	0.809	0.588−1.115	0.195
Nonparoxysmal atrial fibrillation	1.838	1.214−2.781	0.004
Left atrial volume index (ml/m^2)	1.022	1.013−1.031	<0.001

regurgitation can cause left atrium enlargement, leading to AF and, due to the increase in left atrial size, a higher risk of AF recurrence after PVI.[18]

Due to fact that significantly more patients with paroxysmal AF than nonparoxysmal AF receive cryo-ablation treatment, we consider LAVI to be a clinically more relevant predictor of AF recurrence than the type of AF, allowing for risk stratification within the group of paroxysmal AF ablation patients.[19]

Although LA diameter is a widely used parameter in studies on AF, it has been shown that left atrial volume, measured by cardiac CT or cardiac MRT (cMRT), is superior concerning the accuracy and reliability of the measurement, as well as its prognostic power.[20,21] Furthermore, echocardiographic measurements, cCT and cMRT imaging results differ significantly and do not allow for comparisons of absolute values between studies.[22−24] Physiological LAVI values, derived from cCT data, range between 46.7 ± 10.7[21] to 54.4 ± 11.9[24] ml/m^2. The herein calculated prognostic, cCT-derived LAVI cut-off value of 51.99 ml/m^2 therefore seems to be on the high end of physiological ranges.

Costa and colleagues have calculated 2 optimal prognostic cCT-derived LAVI cut-off values, 54.9 ml/m^2 for paroxysmal AF patients and 70.2 ml/m^2 for patients with nonparoxysmal AF[19]. Abecassis et al.[25] noted that the probability of AF recurrence was significantly elevated in AF patients with cCT-derived LAV of ≥100 ml (compared with 98.50 ml in our analysis), yet found the optimal cut-off value to be 145 ml. D'Ambrosio et al.[26] have found a cut-off value of 57 ml/m^2 (combined with age and gender as the "ZAQ score") to be predictive of LA low voltage

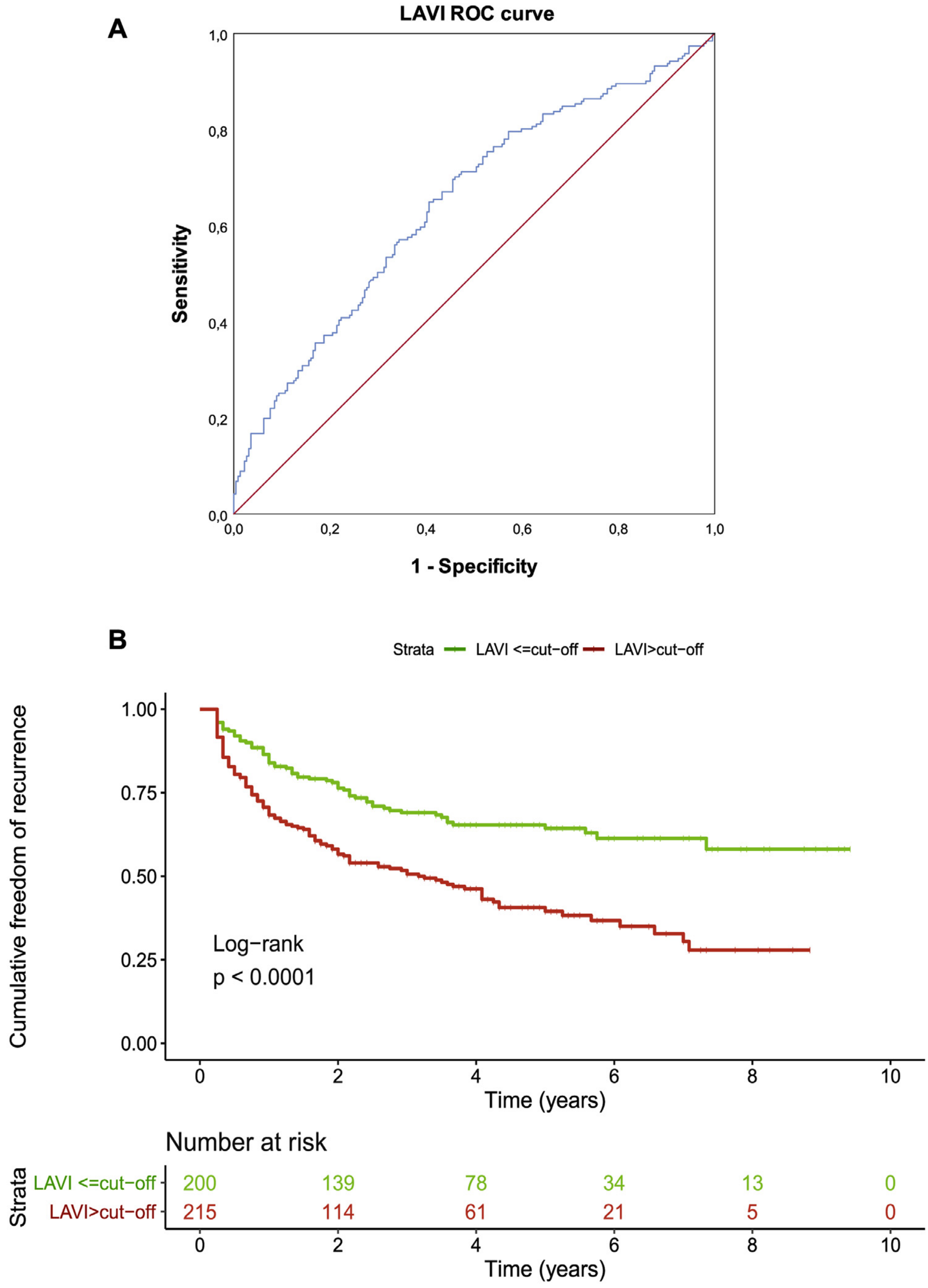

Figure 3. (A) Receiver operating characteristic (ROC) curve of the variable LAVI. (B) Kaplan-Meier survival curve of the patient population divided according to the calculated predictive LAVI cut-off value. LAVI: left atrial volume index.

areas. These differences indicate that, for future prospective studies and scores, it might be appropriate to use a (narrow) range rather than 1 fixed value as a cut-off.

The results highlight that cryo-ablation procedures are effective in the management of drug-refractory AF. Many studies and guidelines emphasize that repeat ablation procedures, following the index procedure, can additionally bolster the success rate significantly.[12,27] Cardiac CT-derived LAVI has been shown to be an adequate parameter to stratify patients according to their risk of recurrence and should be used more frequently in clinical practice as a prognostic marker and to individualize treatment approaches. Recent studies have shown that higher LAVI is oftentimes associated with cardiac remodelling, thus necessitating an adapted ablation strategy for improved results.[26]

This study is subjected to several limitations. It reports results from a single centre with the inherent limitations of retrospective data analysis. A limited number of patients with nonparoxysmal AF precludes a meaningful statistical comparison between AF forms and outcomes. Due to the fact that only ablation-naïve patients were included, the inclusion period is relatively long-still, only 3 experienced interventionalists conducted all the herein analysed procedures. Concerning follow-up, close monitoring of the patients ended after 1 year. Even though the conducted long-term follow-up was thorough, recent investigations suggest that occurrences of asymptomatic AF recurrence might have been missed.[28] Only future, prospective studies might confirm the herein calculated cCT LAVI cut-off value concerning appropriateness, reliability, and clinical relevance.

In conclusion, long-term success and complication rates of cryo-ablations in our patient cohort were comparable to those of RF ablations. LAVI, calculated form cardiac CT data, was an effective predictor of AF recurrence. Future prospective studies may use the herein calculated cut-off values to stratify their patient cohorts. Current risk scores for AF recurrence or progression risks[29] might underemphasize the importance of LAVI as a predictive factor.

Authors contribution

Julian Maier, M.D.: Conceptualization, Methodology, Formal analysis, Investigation, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualization.

Hermann Blessberger, M.D.: Conceptualization, Methodology, Formal analysis, Investigation, Data Curation, Writing - Review & Editing, Supervision.

Alexander Nahler, M.D.: Conceptualization, Methodology, Investigation, Writing - Review & Editing, Supervision.

Denis Hrncic, M.D.: Conceptualization, Investigation, Writing - Review & Editing.

Alexander Fellner, M.D.: Conceptualization, Investigation, Writing - Review & Editing.

Christian Reiter, M.D.: Conceptualization, Investigation, Writing - Review & Editing.

Simon Hönig, M.D.: Conceptualization, Investigation, Writing - Review & Editing.

Pierre Schmit, M.D.: Conceptualization, Investigation, Writing - Review & Editing.

Franz Fellner, M.D.: Conceptualization, Investigation, Writing - Review & Editing.

Thomas Lambert, M.D.: Conceptualization, Methodology, Investigation, Writing - Review & Editing, Supervision.

Clemens Steinwender, M.D.: Conceptualization, Methodology, Investigation, Writing - Review & Editing, Supervision.

Declaration of Interests

The authors declare that they have no known competing financial interests or personal relations that could have appeared to influence the work reported in this study.

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Supplementary materials

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