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LOCAL CAPTURES OF THE PULMONARY VEIN MYOCARDIUM ARE A PREDICTOR OF IMPROVED
LONG-TERM RESULTS OF RADIOFREQUENCY ABLATION OF NONPAROXYSMAL
ATRIAL FIBRILLATION

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Aim. To evaluate the prognostic value of local captures after pulmonary vein isolation in patients with nonparoxysmal atrial fibrillation (AF) for the long-term results of radiofrequency ablation (RFA).

Methods. A single-center observational prospective study. The total number of patients 110. All patients underwent primary catheter ablation for nonparoxysmal AF. During the operation, the activity of pulmonary veins and the presence of local captures were assessed. Patients with local captures in at least one pulmonary vein were included in the first group. Patients who had no local captures were included in the second group. The number of patients in the first group is 54 patients, the number of patients in the second group is 56 patients. The groups had no statistically significant differences in the main indicators -gender, weight, age, duration of medical history, volume of the left atrium and left ventricular ejection fraction, as well as in concomitant pathology. The time of RFA and fluoroscopy, and the duration of operations between the groups also had no statistically significant differences.

Results. The follow-up period was 800 [286.5;800] days. The overall effectiveness of the treatment was 68.2% (75 patients out of 110), considering repeated operations. In the group with local captures, sinus rhythm was maintained at the end of the follow-up period in 42 out of 54 patients (77,7%), in the group without local captures in 33 out of 56 patients (58,9%). The difference is statistically significant (odds ratio 2,439 (95% confidence interval 1,060 -5,615 p=0,034). The presence of local captures in the construction of a multifactorial logistic regression model is a predictor of the effectiveness of RFA ($\chi^2=14,710$; p=0,012).

Conclusion. In this study, local captures in the pulmonary veins in patients with nonparoxysmal atrial fibrillation were a predictor of improved long-term results of radiofrequency ablation.

Key words: nonparoxysmal form of atrial fibrillation; radiofrequency ablation; local captures; predictors of effectiveness; pulmonary veins

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Atrial fibrillation (AF) is the most common arrhythmia in the human population, increasing the risks of stroke and adverse cardiovascular outcomes [1]. The effectiveness of AF treatment remains far from optimal, particularly in patients with non-paroxysmal forms [2]. Randomised clinical trials have demonstrated that catheter ablation is more effective than pharmacological therapy, reducing the risk of AF recurrence and improving patients' quality of life. Moreover, it may positively influence survival in patients with congestive heart failure [3-5].

AF is typically initiated by triggers and subsequently sustained by various mechanisms over time. Ectopic activity, especially originating from the pulmonary veins (PVs), plays a central role in AF initiation [6]. Myocardial in the PVs are extensions of the left atrial (LA) myocardium containing cells with the capacity for

spontaneous depolarisation [7]. These cover the distal segments of the PVs. Compared with LA myocardium, PV myocardial exhibit slower conduction, a shorter effective refractory period, and greater susceptibility to AF induction during programmed electrical stimulation [8]. These electrophysiological properties make PVs an arrhythmogenic substrate responsible for the initiation and maintenance of AF.

PV respond to electrical stimulation, and the resulting electrical activity can be recorded and quantified. During pacing, local electrical signals occurring after the pacing artefact can be detected by a circular catheter positioned at the PV ostium. These signals, termed local captures (LCs), reflect electrical activity arising in close proximity to the catheter. Since PV are relatively small in volume, the electrical activity induced by pacing may not always be detectable [9]. The prognostic role of LCs in

interventional AF treatment has not been extensively studied.

We hypothesised that the presence of LCs in isolated PVs indicates a larger myocardial mass and, consequently, a greater role in AF initiation and maintenance. Thus, in patients with non-paroxysmal AF, the detection of LCs after PV isolation may signify a higher probability of eliminating both triggering and sustaining mechanisms of AF. Conversely, the absence of LCs may serve as a surrogate marker of advanced fibrotic remodelling of the LA, reducing the likelihood of long-term sinus rhythm maintenance after catheter ablation. Therefore, the presence of LCs may act as a predictor of AF ablation outcomes.

Aim: to assess the prognostic significance of local captures after PV isolation in patients with non-paroxysmal AF in relation to the long-term outcomes of radiofrequency catheter ablation (RFCA).

METHODS

This was a single-centre, prospective, observational study conducted between April 2021 and April 2022.

Inclusion criteria:

- Non-paroxysmal AF (persistent or long-standing persistent, as defined by the expert consensus [1]);
- Symptomatic AF refractory to antiarrhythmic therapy (AAT) (at least one class IC or class III drug) or intolerance to AAT;
- First RFCA procedure;
- Adequate anticoagulation (target INR 2.0-3.0 in patients on warfarin or direct oral anticoagulant therapy);
- Absence of significant valvular heart disease;
- Age 40-75 years.

Exclusion criteria:

- Coexistence of AF with typical or atypical atrial flutter;
- LA diameter >60 mm on echocardiography (Echo);
- History of cardiac surgery for mitral valve disease;
- Reversible causes of AF;
- LA appendage thrombus.

Baseline characteristics of patients

	All patients (n=110)	First group LA(+) (n=54)	Second group LA(-) (n=56)	p
Age (years)	60.8±9.1	59.8±9.5	61.8±8.6	0.256
Male sex, n (%)	70 (63.6%)	38 (70.4%)	32 (57.1%)	0.152
BMI, kg/m ²	30.4±4.6	30.0±4.5	30.8±4.6	0.349
LVEF, %	56.1±9.3	55.2±9.8	57.1±8.7	0.293
LA volume, mL	101.8±30.7	97.8±26.7	105.8±33.8	0.169
LA diameter, mm	43.4±5.6	42.9±5.4	43.8±5.8	0.404
AA, months	36 (12;72)	42 (12;75)	36 (10;69)	0.472
PD, months	6.0 (3.0;10.25)	6.0 (2.0;9.5)	6.0 (2.5;10.0)	0.642
DM, n (%)	14 (12.7)	10 (18.5)	4 (7.1)	0.075
AH, n (%)	97 (88.2)	51 (94.4)	48 (85.7)	0.082
IHD, n (%)	16 (14.5)	8 (14.8)	8 (14.3)	0.938

Note: BMI - body mass index; LVEF - left ventricular ejection fraction; LA - left atrium; ADA - arrhythmic anamnesis; PD - persistence duration; DM - diabetes mellitus; AH - arterial hypertension; IHD - ischaemic heart disease.

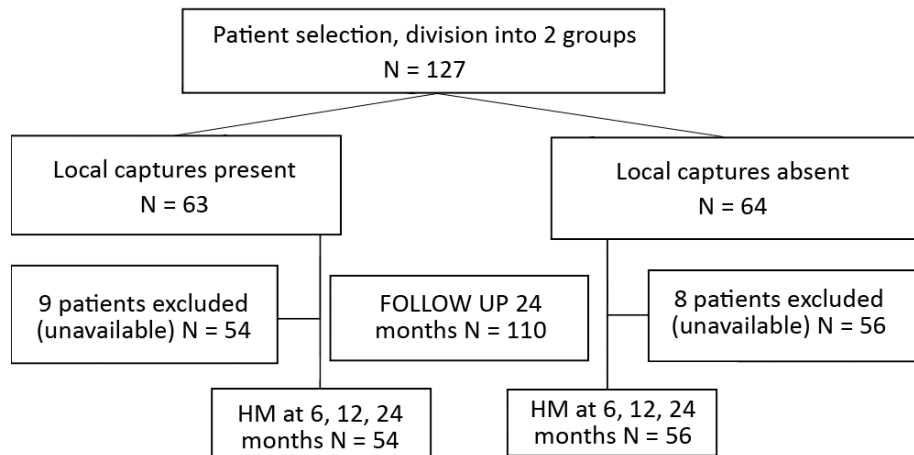


Fig. 1. Study design, where HM - Holter monitoring.

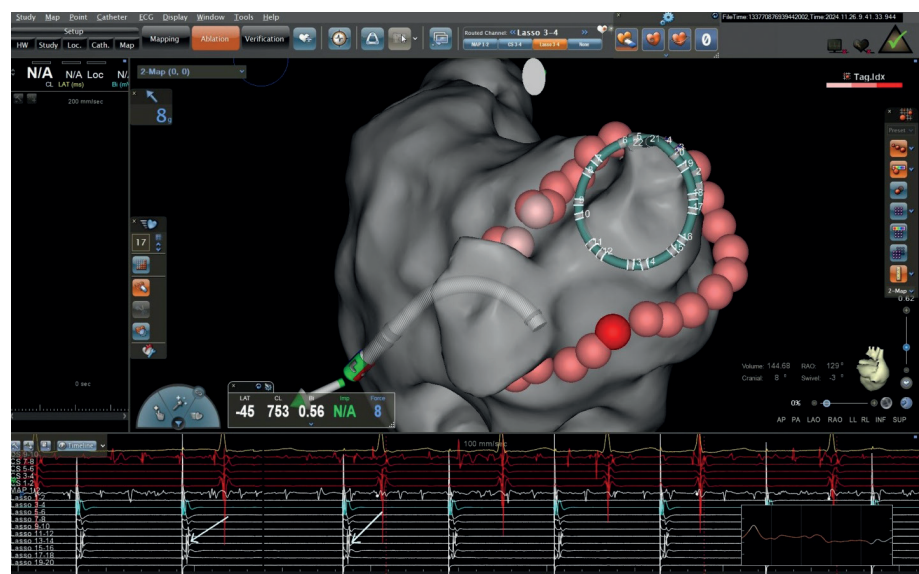


Fig. 2. Local captures in the right superior pulmonary vein. White arrows indicate local captures recorded on the Lasso catheter. The “Tissue Proximity Indication” module (white markers identifying the electrodes on the Lasso catheter) shows tight electrode contact with the pulmonary vein tissue.

A total of 127 patients undergoing first RFCA for persistent or long-standing persistent AF were enrolled. The patients were divided into two groups: Group 1 included those with LCs after PV isolation (63 patients), and Group 2 consisted of patients without LCs (64 patients). Seventeen patients were excluded due to inability to complete follow-up (9 from Group 1, 8 from Group 2). Thus, the final analysis included 110 patients: 54 in Group 1 and 56 in Group 2 (Fig. 1). The groups showed no statistically significant differences in baseline characteristics, including age, sex, body weight, AF history, comorbidities, LA volume, or left ventricular ejection fraction (Table 1).

Prior to the procedure, all patients underwent either transoesophageal echocardiography (TEE) or contrast-enhanced cardiac computed tomograph to exclude LA appendage thrombus. Procedures were performed under intravenous sedation. Patients remained responsive throughout the intervention. Dexmedetomidine was used for sedation, and fentanyl for analgesia.

Catheterisation of the coronary sinus with a multipolar catheter was performed via femoral or subclavian venous access, depending on operator preference. Double transseptal puncture was performed under fluoroscopic guidance without TEE. Two non-steerable introducers were advanced into the LA. To achieve target activated clotting time (ACT >300 seconds), an intravenous bolus of heparin was administered. Heparin dosing depended on anticoagulant therapy: patients on direct oral anticoagulants received a higher heparin dose compared with those on warfarin (17.9±4.4 thousand IU vs. 14.8±5.1 thousand IU, respectively) [10]. Target ACT values were subsequently maintained with continuous heparin infusion.

Table 2.

Main characteristics of the procedures performed

	First group N=54	Second group N=56	P
Procedure time, min	108±27,2	101,9±26,9	0,194
Fluoroscopy time, s	164,1±77,7	170,7±96,5	0,695
RFA time, min	32,2±10,3	29,8±9,9	0,213

Note: RFA - radiofrequency ablation

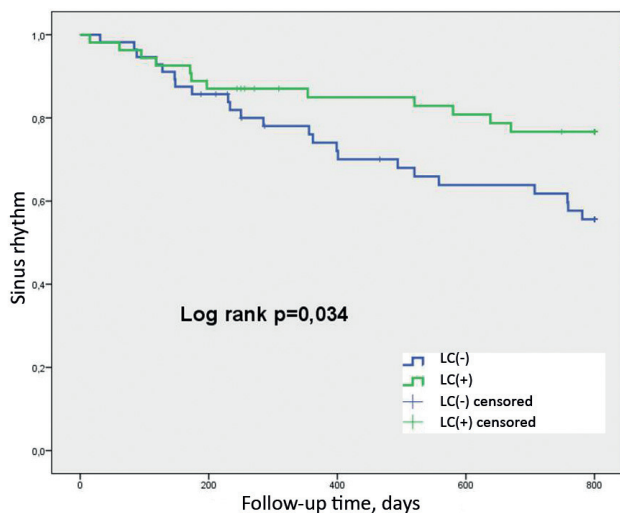


Fig. 3. Maintenance of sinus rhythm in the first and second patient groups.

Oesophageal position was visualised with contrast oesophagography using Omnipaque (GE Healthcare Ireland). A 20-pole Lasso® catheter (Biosense Webster, Johnson & Johnson, USA) was used to construct LA anatomical maps with the CARTO 3 system (Biosense Webster, Johnson & Johnson, USA). PV activity was assessed with the Lasso catheter. The catheter depth was confirmed fluoroscopically, with positioning at the cardiac contour in LAO 30° projection for the left PVs and RAO 30° for the right PVs. If no spike activity was recorded inside a vein, the vein was considered electrically inactive.

Following the CLOSE protocol [11], PV ostial isolation was performed with EZ Steer Nav SmartTouch catheters (Biosense Webster, Johnson & Johnson, USA). RF applications were delivered using a Stockert RF generator (Biosense Webster, Johnson & Johnson, USA) in power-control mode. Maximum RF power was 40 W. Irrigation with saline was performed using the CoolFlow pump (Biosense Webster, Johnson & Johnson, USA) at 30 ml/min.

On the posterior LA wall adjacent to the oesophagus, RF power was limited to 30 W with a maximum duration of 10 seconds. RF application points were annotated using CARTO 3 Visitag settings: contact force >4 g for at least 35% of the application time and catheter tip displacement ≤2.5 mm. The distance between neighbouring ablation points was ≤6 mm. The ablation index (AI) targets were 450 for the anterior wall and 300 for the posterior wall. These thresholds were established by Biosense Webster specialists for our centre after reviewing 10 blinded PV isolation procedures [12].

After isolation of the right and left PVs, the Lasso catheter was placed sequentially in each PV. The Carto 3 “Tissue Proximity Indication” module was used to assess electrode-tissue contact. Stimulation was delivered from all electrode pairs with a current of 10 mA and pulse duration of 1 ms. Endograms were analysed for the presence of LCs by two physicians. If their opinions coincided, the LC was considered present (Fig. 2). Any disagreement or doubt by at least one of the experts was interpreted as absence of LCs. Statistics on inter-observer disagreement were not collected.

If the patient was in sinus rhythm at the time of the procedure, the intervention was limited to PV isolation alone. In cases where AF was ongoing during the procedure, some patients—at the operator’s discretion—in addition to PV isolation underwent AF substrate modification, which involved identifying and ablating atrial myocardium regions with spatiotemporal dispersion of activation [13]. There was no standardised lesion set in the LA; additional ablations were tailored individually to each patient depending on the localisation of dispersion zones. If sinus rhythm was not restored, external cardioversion was performed. Entrance and exit block of all PVs was then reassessed.

One case of haemopericardium occurred in a patient from Group 2, which resolved after pericardial drainage. No other complications were observed. All patients continued antiarrhythmic therapy for 4 weeks after RFCA. Discontinuation of antiarrhythmic drugs was at the discretion of the attending physician depending on the clinical situation. Anticoagulant therapy was not discontinued regardless of procedural efficacy.

Postoperative follow-up was performed both in person and remotely. Some patients were seen on schedule at the outpatient clinic, where clinical status was assessed and Holter monitoring (HM) performed. Patients from remote regions submitted medical documentation including symptom reports and HM data at 6, 12, and 24 months after RFCA. Recurrence of arrhythmia was defined as any documented AF or atrial tachycardia lasting longer than 30 seconds. In such cases, patients were referred for repeat ablation. The primary endpoint was the absence of atrial arrhythmias at the end of follow-up, accounting for repeat interventions.

Statistical Analysis

Statistical analysis was performed using IBM® SPSS® Statistics (Version 20, 2011). Normality of distribution was assessed using the Kolmogorov-Smirnov test. For normally distributed data, results are presented as arithmetic mean $\pm$ standard deviation ($M \pm SD$) with 95% confidence interval (95% CI). For non-normally distributed data, results are expressed as median and interquartile range. For comparisons of means, the Student's t-test was used for normally distributed data, and the Mann-Whitney test for non-normally distributed data. Treatment efficacy was evaluated using the Kaplan-Meier method, with differences compared using the two-sided log-rank test.

Multivariate regression modelling was performed using the binary logistic regression module. Parameters whose predictive role for RFCA efficacy was demonstrated in univariate analysis at a significance level of $p < 0.1$ were included in the regression analysis. The decision to retain a predictor in the model was based on the Wald statistic. The enter method was applied to include variables simultaneously into the equation. Model performance was evaluated using ROC analysis. A critical level of statistical significance of $p < 0.05$ was assumed when testing hypotheses.

RESULTS

In the first group (LC+), AF was recorded intraoperatively in 90.7% of patients (49), while 9.3% (5 patients) were operated in sinus rhythm. In the second group (LC-), 85.7% (48 patients) underwent the procedure during AF, and 14.3% (8 patients) in sinus rhythm. The difference between groups was not statistically significant ($p = 0.652$). In the first group, PV isolation without additional LA interventions was performed in 51.9% (28 patients), compared with 46.4% (26 patients) in the second group ($p = 0.574$). Isolation of PV ostia was achieved in 100% of patients.

In the LC+ group, the majority of PVs were active (213 of 216, 98.6%), whereas in the LC- group the proportion of active PVs was lower (174 of 224, 77.7%). This difference was statistically significant ($p < 0.05$).

No significant differences were observed in the main procedural characteristics between the two groups (Table 2). Spontaneous ectopic activity in isolated PVs was observed only in the LC+ group, recorded in 25 PVs of 19 patients; in the LC- group no ectopic PV activity was noted ($p < 0.05$). The distribution of PVs with ectopic activity was as follows: right superior PV - 15 cases, left superior PV - 7 cases, left inferior PV - 2 cases, right inferior PV - 1 case. In all cases with ectopic activity in a PV, LCs were simultaneously detected in the same PV (100%).

The frequency of LCs coincided with the frequency of ectopic PV activity. LCs were recorded in the right superior PV in 44 cases, left superior PV in 36, left inferior PV in 15, and right inferior PV in 12. LCs were detected in all four PVs in 1 patient (1.9%), in three PVs in 14 patients (25.9%), in two PVs in 22 patients (40.7%), and in one PV in 17 patients (31.5%). Among patients with LCs in one PV, RFCA efficacy was 75%. Patients with LCs in two or three PVs demonstrated similar efficacy - 64.3% and 65.2%, respectively. The single patient with LCs in all four PVs experienced AF recurrence after 580 days of follow-up. No statistically significant difference in treatment efficacy was observed according to the number of PVs with LCs ($p = 0.317$). PVs with LCs were completely isolated in 100% of cases, both during sinus rhythm and AF.

Of the total cohort, 46 patients (41.8%) were followed up in person and 64 patients (58.2%) remotely. Maintenance of sinus rhythm after RFCA was achieved in 31 patients (67.4%) with in-person follow-up and in 44 patients (68.8%) with remote follow-up; this difference was not statistically significant ($p = 0.621$).

The median follow-up period was 800 [286.5; 800] days. Overall treatment efficacy in the entire cohort was 68.2% (75 of 110 patients). Repeat procedures were performed in 12 patients (22.2%) in the LC+ group and in 19 patients (33.9%) in the LC- group, with no significant difference between groups ($p = 0.122$). During repeat procedures, reconnection in at least one PV was observed in all LC+ patients, while in the LC- group PV isolation persist-

Table 3.

Data from univariate and multivariate regression analysis

	Univariate regression			Multivariate regression		
	OR	95%CI	P	OR	95% CI	P
Age (years)	1.162	0.223-6.145	0.859			
Male sex, n (%)	1.500	0.689-3.478	0.344			
BMI, kg/m ²	1.086	0.898-1.875	0.086	1.112	1.005-1.230	0.039
LVEF, %	1.083	0.992-1.095	0.105			
LA volume, mL	1.002	0.984-1.014	0.787			
LA diameter, mm	0.982	0.952-1.067	0.837			
AA, months	0.994	0.984-1.014	0.121			
DP, months	1.173	0.490-2.793	0.719			
DM, n (%)	3.364	0.664-14.03	0.136			
AH, n (%)	1.408	0.989-1.344	0.099	1.779	0.424-7.467	0.431
CAD, n (%)	1.009	0.940-4.707	0.719			
Local captures	0.424	0.178-0.944	0.036	0.293	0.115-0.747	0.010

Note: OR - Odds Ratio; CI - Confidence Interval

ed in 10 patients (52.6%). This difference was statistically significant ($p < 0.05$).

At the end of follow-up, sinus rhythm was maintained in 42 of 54 patients (77.7%) in the LC+ group compared with 33 of 56 patients (58.9%) in the LC- group. This difference was statistically significant, with an odds ratio (OR) of 2.439 (95% CI 1.060-5.615, $p = 0.034$) (Fig. 3).

Univariate regression analysis identified several factors with the strongest predictive potential: body mass index (BMI), arterial hypertension, and the presence of LC (Table 3). Based on these findings, a multivariate regression analysis was performed. Variables (BMI, LC) that demonstrated a statistically significant association with the endpoint were included in the prognostic model. The constructed model was statistically significant ($\chi^2 = 14.710$; $p = 0.012$). The Nagelkerke R^2 was 0.175, and the Hosmer-Lemeshow test result was 0.247. Both univariate and multivariate regression analyses identified the presence of LC as a predictor of long-term sinus rhythm maintenance after RFCA.

The quality of the resulting model was assessed using ROC analysis. The area under the ROC curve (AUC) was 0.70 ± 0.057 (95% CI 0.588-0.813) (Fig. 4). The cut-off value of the function was 0.6058 (sensitivity 73.3%, specificity 63%). The AUC for the new dichotomized variable was 0.718 (95% CI 0.611-0.814). After adjusting the classification threshold according to ROC analysis, the diagnostic performance of the multivariate model reached 70% (sensitivity 78.3%, specificity 65%).

DISCUSSION

The results of interventional treatment in patients with persistent AF remain suboptimal. Numerous attempts to improve efficacy by adding additional lesions to PV isolation initially yielded promising outcomes in pilot studies [14]. However, large randomized multicentre trials failed to demonstrate any advantage of additional LA lesions compared with PV isolation alone [15]. Thus, the optimal ablation set for patients with persistent AF has not yet been

established. Persistent AF is likely to involve multiple underlying electrophysiological mechanisms, and identifying the dominant mechanism in each individual patient is critical for designing a tailored ablation strategy [16]. Unlike paroxysmal AF, which is predominantly trigger-driven, persistent AF is largely substrate-dependent. One limitation of substrate modification is the difficulty of identifying patients who may benefit from this approach. This makes it challenging to propose a standardized and, more importantly, reproducible ablation strategy for persistent AF [17].

One potential option for individualising interventional treatment in non-paroxysmal AF is to determine the extent of ablation based on the presence or absence of LCs in isolated PVs. It is well established that the more advanced the degree of fibrosis in the LA, the higher the likelihood of AF recurrence after catheter ablation [18, 19]. The absence of LCs may therefore serve as a surrogate marker of fibrotic remodelling not only in the LA myocardium but also in the PV myocardial. In such cases, the role of PVs in initiating and maintaining persistent AF may be minimal, and achieving clinical success may require more extensive ablation within the LA. Conversely, the presence of LCs may indicate a greater involvement of PVs in sustaining AF, and their isolation alone might be sufficient to maintain sinus rhythm. Unfortunately, in this study, no direct assessment of LA fibrosis or its relationship with LC presence/absence was performed, and this issue requires further investigation.

The relationship between LC presence and the effectiveness of interventional treatment across different AF types remains poorly understood. The literature contains limited data on the prognostic role of LCs in catheter procedures, with most publications describing their use as a convenient marker of achieved PV isolation [20]. The authors identified only one published study, by A. Babak et al. (2024) [21], which investigated the electrophysiological properties of PVs after cryoballoon ablation in 390 patients with different AF types, and their impact on long-term outcomes. In patients with persistent AF, LCs were observed in 17.1% of cases, compared with 49.1% in our study. The use of the Carto 3 system's Tissue proximity indication module may have allowed us to ensure denser electrode-tissue contact, thereby optimising conditions for sleeve stimulation and LC detection. Patients with persistent AF who demonstrated LCs after PV isolation achieved higher rates of sinus rhythm maintenance than those without LCs. The authors therefore also proposed the use of LCs as a factor guiding ablation strategy in patients with persistent AF. Our findings were consistent with these results, despite differences in the type of ablation energy used.

The assumption that LCs reflect greater PV arrhythmogenicity has been supported in patients with paroxysmal AF [9]. Patients with LCs showed greater RFCA efficacy than those without. Although LCs are not generally considered a mandatory criterion for successful PV isolation, their presence has been described as a favourable prognostic sign [22]. Of particular interest is the study by F. Marshlinski et al. [23], which considered the disappearance of LCs after PV isolation as a marker of durable isolation. That study involved 30 patients undergoing

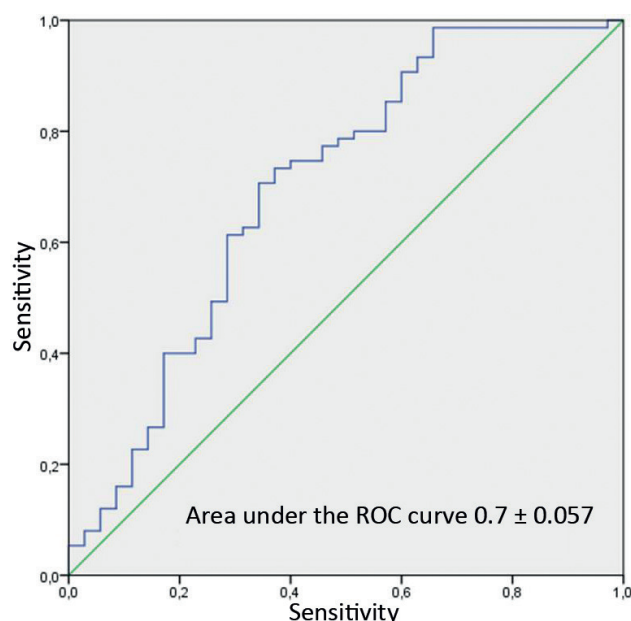


Fig. 4. ROC curve of the multivariable logistic regression model.

primary or repeat PV isolation. Before ablation, 99.8% of PVs exhibited LCs, while after ablation LCs persisted in only 60.9% of PVs. The absence of LCs correlated with a lower likelihood of reconnection during adenosine testing (4% in PVs without LCs versus 23% in PVs with LCs). Although the article did not provide a clear electrophysiological explanation for LC disappearance after PV antral isolation, the authors hypothesised that PVs losing LC had thinner myocardial. Antral ablation lines might also have damaged ganglionated plexuses or fibres projecting to PVs, thereby reducing sleeve excitability and abolishing LCs. They proposed LC disappearance as a marker of reliable PV isolation.

In our study of patients with persistent AF, the presence of LCs after PV isolation was a predictor of RFCA efficacy. In all LC+ patients undergoing repeat RFCA procedures, reconnection was observed in at least one PV. By contrast, in more than 50% of LC- patients PV isolation was preserved, yet RFCA efficacy was lower compared with the LC+ group. This may be explained as follows: in LC+ PVs, the greater myocardial sleeve mass likely contributes more to AF initiation and maintenance, making reconnection in these veins more

arrhythmogenic. In contrast, LC- PVs contain fewer myocardial fibres, reducing arrhythmogenic potential and increasing the likelihood of durable isolation. Thus, reconnection in LC+ PVs may confer a higher risk of AF recurrence than reconnection in LC- PVs. These findings suggest that, when LCs are present, more stringent verification of PV isolation may be warranted, including the use of concealed conduction testing.

Study Limitations

The limitations of this study include its single-centre design and the relatively small sample size. In addition, the assessment of LC requires specific technical expertise, which may complicate the interpretation of the findings. Furthermore, the absence of data on interobserver variability in evaluating the presence of LC may have introduced bias, potentially leading to an overestimation of their frequency.

CONCLUSION

In this study, local captures (LCs) in the pulmonary veins (PVs) of patients with non-paroxysmal atrial fibrillation (AF) were predictors of improved long-term outcomes after radiofrequency ablation (RFA).

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