Local epicardial robotic-enhanced hybrid ablation efficacy predictors for persistent atrial fibrillation

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BACKGROUND Hybrid ablation can manage persistent atrial fibrillation (PsAF) and long-standing persistent atrial fibrillation (LSPAF). Robotic-enhanced hybrid ablation (RE-HA) offers greater precision and stability. However, biophysical predictors of effective local epicardial radiofrequency ablation (ELRF) during epicardial ablation are unknown.

OBJECTIVE The purpose of this study was to compare the time course of biophysical predictors of ELRF and no-ELRF during the first stage of RE-HA in patients with PsAF and LSPAF.

METHODS We conducted a dual-center retrospective cohort study involving 92 consecutive patients with PsAF or LSPAF who underwent RE-HA between January 2021 and May 2024. Epicardial electrogram disappearance, defined as a reduction of bipolar voltages to <0.05 mV, baseline impedance (BI), and impedance drop (ID), were compared between ELRF and no-ELRF cases. Univariate and multivariate logistic regression models were used to identify predictive variables. Optimal cutoff values were determined using receiver operating characteristic curves.

RESULTS Among 2474 radiofrequency (RF) applications, significant predictors of ELRF included BI and ID at 1 and 8 seconds, with optimal cutoff values of <107, 0–7, and 5–17 Ω. The composite predictive model had an area under the receiver operating characteristic of 0.775, with 94% sensitivity, 53% specificity, and 65% accuracy. Our predictive ELRF score ranged from 0–4, and the Youden J test identifying a cutoff value of 3 as optimal.

CONCLUSION BI and progressive ID were strong predictors of local epicardial RE-HA efficacy. The composite model was a reliable tool for early identification of ELRF, potentially reducing RF delivery and enhancing procedural efficiency. Larger prospective studies are needed to validate these findings.

KEYWORDS Electric impedance; Persistent atrial fibrillation; Long-standing persistent atrial fibrillation; Retrospective studies; Robotic surgical procedures; Impedance drop; Baseline impedance; Left atrial appendage; Robotic-enhanced hybrid ablation; Catheter ablation

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Introduction

Pulmonary vein isolation (PVI) is the cornerstone of all atrial fibrillation (AF) ablation strategies. However, this procedure is less effective for patients with persistent atrial fibrillation (PsAF) or long-standing persistent atrial fibrillation (LSPAF).[1–5]

The success rate of the first procedure in these patients is only 43%, which necessitates comprehensive treatment of other areas in addition to PVI.[6–9] The latest guidelines recommend hybrid AF ablation for patients with PsAF and LSPAF.[10–12] Hybrid AF ablation combines thoracoscopic epicardial surgical ablation with endocardial catheter ablation and offers advantages, such as confirmation of PVI and creation of additional lesions on the endocardial side.

We recently demonstrated that epicardial, robotic-enhanced hybrid ablation (RE-HA) is a feasible, less

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KEY FINDINGS

- Epi-Sense probe's sensing electrodes can be used to assess baseline impedance (BI) and impedance drop (ID) during robotic-enhanced hybrid ablation for persistent and long-standing persistent atrial fibrillation.
- Focusing on complete signal dropout after radiofrequency (RF) application and ablation parameters, baseline BI and progressive and stable ID scores at 1–8 seconds were the primary predictors of effective local epicardial radiofrequency ablation (ELRF).
- Early impedance parameters can accurately predict acute ELRF, potentially reducing RF delivery and enhancing procedural efficiency.

invasive, and safe novel surgical approach effective for patients with PsAF or LSPAF.[13,14]

Several strategies have been developed to guide radiofrequency (RF) energy delivery and assess the completeness of the resulting lesion sets. During radiofrequency ablation (RFA), impedance is defined as the resistance encountered by the current passing from the catheter tip to the myocardium. An impedance drop (ID) resulting from RF delivery is a real-time marker of tissue heating and has been associated with effective lesion formation during endocardial RFA.[15,16]

However, over time, impedance may increase and IDs may become unstable, which reflect catheter movement, poor catheter–tissue contact, or charring without effective lesion formation.[17] Impedance behavior during epicardial RE-HA and its value as a predictive parameter have not yet been evaluated.

This study aimed to investigate the time course of impedance behavior and to identify the parameters that best predict effective local epicardial radiofrequency ablation (ELRF) during the initial stages of epicardial RE-HA in patients with PsAF and LSPAF. Particularly, we assessed the relationship between impedance and the disappearance of epicardial electrograms (EGMs). Additionally, we developed a practical scoring system to identify effective and ineffective local epicardial applications within the initial seconds, potentially minimizing RF delivery.

Methods

Study population

This retrospective dual-center study included consecutive patients with documented PsAF, defined as continuous sustained beyond 7 days, or LSPAF, defined as continuous AF for >12 months, who underwent epicardial RE-HA between January 2021 and May 2024 at Humanitas Gavazzeni, Bergamo, Italy, and the Medical College of Wisconsin, Milwaukee, Wisconsin. The study was approved by the institutional review boards of both institutions and adhered to the ethical principles outlined in the Declaration of Helsinki (ethics committee of IRCCS Humanitas Clinical Institute Rozzano, Italy, Prot. 32/23 GAV, September 19, 2023). All patients provided written informed consent.

According to European Society of Cardiology guidelines, eligible participants are between the ages of 18 and 75 years, with symptomatic PsAF or LSPAF, who met at least 2 of the following criteria[12]: (1) no response or intolerance to at least 2 classes of antiarrhythmic drugs; (2) previously failed percutaneous AF ablation procedures; and (3) evident risk factors for AF recurrences after transcatheter ablation, including body mass index >30 kg/m^2, left atrial volume index >40 mL/m^2, and AF duration >24 months. Exclusion criteria were (1) previous surgical ablation; (2) acute myocardial infarction; (3) coronary artery bypass graft, coronary or carotid stenting, or endarterectomy within the previous 6 months; (4) any surgical intervention within the preceding 3 months; (5) left atrial thrombus demonstrated by preprocedural imaging tests, such as transesophageal echocardiography, magnetic resonance imaging, or computed tomographic scan; (6) left ventricular ejection fraction <40%; (7) thromboembolic event, such as transient ischemic attack, ischemic stroke, and pulmonary embolism, within the past 12 months; (8) uncontrolled heart failure New York Heart Association functional class III or IV; and (9) unfeasible single lung ventilation.

Procedural protocol

All epicardial RE-HA procedures were performed using the Da Vinci Xi system (Intuitive Surgical Inc, Sunnyvale, CA) and a unilateral left-sided thoracoscopic approach with patients under general anesthesia through double-lumen endotracheal intubation for selective right lung ventilation. We used a combination of midazolam for anxiolysis, and fentanyl, propofol, rocuronium, lidocaine, ketamine, and magnesium sulfate for induction of general anesthesia. An esophageal temperature probe (S-Cath Esophageal Temperature Probe, Circa Scientific, Englewood, CO) was placed to continuously monitor for potential retrocardiac spread of thermal energy, with a maximum accepted threshold of 37.2°C. After left lung deflation, 4 robotic ports (three with 8-mm diameter and one with 12-mm diameter) were inserted in a hockey-stick configuration through the third, fifth, eighth, and seventh left intercostal spaces, respectively.[13,14] The first port houses the robotic camera, providing high-definition visualization of the surgical field. Two additional ports accommodate robotic instruments, allowing precise manipulation and dissection, with careful arm separation to avoid collisions. The fourth port, a 12-mm AirSeal port, serves as the bedside assistant port, facilitating instrument exchange. This configuration ensures efficient workflow and enhances the safety and precision of the procedure. A complete epicardial lesion set (Supplemental Figure 1) included (1) bilateral semicircumferential pulmonary vein ablation; (2) complete box lesion set to connect the lesions among all pulmonary veins; (3) ablation of the left atrial posterior wall, excluding the area

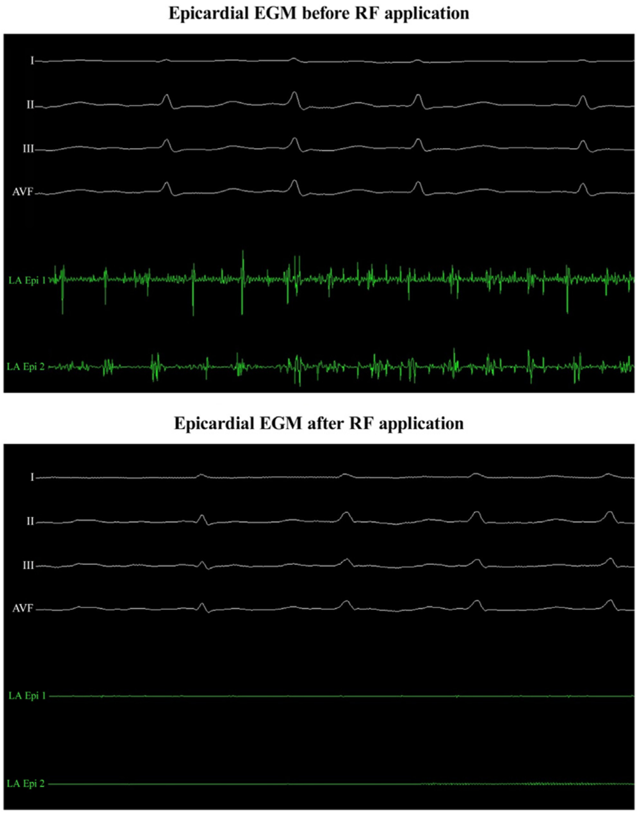

Figure 1 Example of complete signal dropout after radiofrequency (RF) application. Electrograms (EGMs) before **(top)** and after **(bottom)** effective energy application are shown.

under the pericardial reflection; (4) transection of the ligament of Marshall; (5) ablation of the left atrial ridge from the left atrial appendage to the left superior pulmonary vein; and (6) exclusion of the left atrial appendage using an epicardial clip (AtriClip PRO2 or PRO-V devices, AtriCure, Inc, Mason, OH).

Unipolar, suction-assisted RFA was performed using a 3-cm closed-irrigation probe (Epi-Sense, AtriCure), which continuously monitored RF energy and impedance every 0.05 second during energy application.

After visual inspection, RF energy was delivered to the standard and intended targets (Supplemental Figure 1) at a standardized preset level of 30 W for 90 seconds to create epicardial lesions and ensure reproducibility of the biophysical data. The probe was cooled by continuous saline perfusion to prevent overheating during ablation. A vacuum seal ensured consistent contact between the closed-irrigation probe and the left atrial tissue. The sensing electrodes of the closed-irrigation probe were connected to a commercial recording system (CardioTek software version number EP-TRACER V1.0.5.12, CardioTek BV, Sittard, The Netherlands) via a CSK-2030 cable (AtriCure) with a 50-Hz pass filter to enable direct transmission of EGMs and enhance the accuracy of lesion assessment. A cardiac electrophysiologist continuously monitored atrial EGMs during RE-HA.

Impedance measurement

During epicardial RE-HA, lesions are created using a vacuum-assisted unipolar RF device (EPi-Sense, AtriCure) set at 30 W for 90 seconds. IDs are monitored as indicators of local tissue destruction, calculated as the difference between the baseline impedance (BI) and the impedance during each application.

ELRF is defined as the completion of a single RF ablation, characterized by the disappearance of the atrial EGM after RF energy application, which is defined as a postablation EGM with a bipolar voltage <0.05 mV (Figure 1).

The primary acute outcome was the disappearance of atrial EGMs (Figure 1). In cases of persistent atrial EGMs, additional applications were administered. Using the AtriCure RF generator, we extracted biophysical data, obtaining 1800 consecutive impedance samples for each RF application within a 90-second period.

For each RF application, ablation parameters included BI, ID, and RF delivery time. All ablation points were exported from the AtriCure RF generator for offline analysis. The EGMs recorded during suction before and after each RF application were stored to analyze the ELRF. For analysis, 4,453,200 ablation parameters were collected.

Sample size calculation

Sample size estimation was based on previously obtained data. Considering approximately 25 energy applications per patient, an *a priori* ELRF of approximately 1/3, a 0.25 proportion of predictor variance due to other covariates and patient differences, a 70%–30% train-test split, and a total of 2250 RF applications, 90 patients were required to provide a power of 85% and a 2-sided alpha error of 0.05 for detecting an odds ratio of 0.75 for a confirmed 10-Ω decrease in ID in the test group. Calculations were performed using the Demidenko formula.

Statistical analysis

Descriptive statistics are given as mean ± SD for continuous variables with normal distribution and as median [interquartile range] for nonparametric variables, as appropriate. Normality was assessed using the Kolmogorov–Smirnov test. Group differences in continuous variables were analyzed using the Student *t* test, whereas categorical variables were compared using the χ^2 test. Univariate analysis of the RF application parameters was performed. After evaluating collinearity using the variance inflation factor score, multivariate analyses using a logistic regression mixed-effects model were performed, using the patient as a random effect. The optimal predictive model was selected using the Akaike information criterion. The intraclass correlation coefficient was used to explain the variance data quantity that was attributable to the differences among patients; values <0.10, 0.10–0.30, 0.30–0.50, and >0.50 were considered negligible, mild, moderate, and high, respectively.

To create, calibrate, and validate the predictive model, the dataset was randomly split into training (70%) and testing

Table 1 Baseline characteristics of patients who underwent epicardial RE-HA

Variables	All patients (N = 92)	Patients with PsAF (n = 60)	Patients with LSPAF (n = 32)	*P* value
Age, y	64 ± 8	63 ± 8	66 ± 9	.105
Male sex	66 (71.7)	45 (75)	21 (65.6)	.479
BMI, kg/m^2	33 ± 6	34 ± 7	31 ± 5	.034
NYHA class				
I	15 (16.3)	12 (20)	3 (9.4)	.309
II	60 (65.2)	37 (61.7)	23 (71.9)	.454
III	17 (18.5)	8 (13.3)	9 (28.1)	.144
IV	0 (0)	0 (0)	0 (0)	1
Arrhythmia history				
Time from the first AF diagnosis (mo) to epicardial RE-HA	68 [25–85]	52 [24–63]	96 [38–105]	.003
AF type				
PAF	0 (0)	0 (0)	0 (0)	1
PsAF	60 (65.2)	60 (100)	0 (0)	<.001
LSPAF	32 (34.8)	0 (0)	32 (100)	<.001
Previous ECV	64 (69.6)	42 (70)	22 (68.8)	.448
CHA_2DS_2-VASc score	3 [2–5]	3 [2–5]	3 [2–5]	.763
HAS-BLED score	2 [1–3]	2 [1–3]	2 [1–3]	.875
Medical history				
Hypertension	62 (67.4)	39 (65)	23 (71.9)	.663
Diabetes	24 (26.1)	18 (30)	6 (18.8)	.357
Dyslipidemia	53 (57.6)	33 (55)	20 (62.5)	.637
Obesity	62 (67.4)	43 (71.7)	19 (59.4)	.335
Thyroid disorders	15 (16.3)	11 (18.3)	4 (12.5)	.671
Obstructive sleep apnea	35 (38.0)	20 (33.3)	15 (50)	.294
Anxiety disorder	11 (12.0)	8 (13.3)	3 (9.4)	.826
Stroke/TIA	7 (7.6)	5 (8.3)	2 (6.3)	.999
Chronic kidney disease	11 (12.0)	5 (8.3)	6 (18.8)	.259
HFrEF	10 (10.8)	6 (10)	4 (12.5)	.988
Coronary artery disease	12 (13.0)	8 (13.3)	4 (12.5)	.999
COPD	6 (6.5)	2 (3.3)	4 (12.5)	.210
Preoperative management of AF				
Class I/III antiarrhythmic drug	75 (81.5)	52 (86.7)	23 (71.9)	.145
Oral anticoagulant	88 (95.6)	57 (91.9)	31 (96.9)	.999
Preoperative echocardiogram				
LV ejection fraction (%)	55 ± 6	57 ± 7	52 ± 5	<.001
LA volume (mL)	124.5 ± 45	117 ± 40	137 ± 52	.043
LA volume index (mL/m^2)	57 ± 21	55 ± 19	61 ± 23	.184
Previous PM/ICD/CRT implantation	12 (13.0)	7 (11.7)	5 (15.6)	.832
Previous sternotomy	3 (3.3)	1 (1.7)	2 (6.3)	.574

Values are given as mean ± SD, n (%), or median [interquartile range] unless otherwise indicated.

AF = atrial fibrillation; BMI = body mass index; CHA_2DS_2-VASc = Congestive heart failure, Hypertension, Age, Diabetes, Stroke, Vascular Disease Score; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; ECV = electrical cardioversion; HAS-BLED = Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly, Drugs/alcohol concomitantly; HFrEF = heart failure with reduced ejection fraction; ICD = implantable cardioverter defibrillator; LA = left atrium; LSPAF = long-standing persistent atrial fibrillation; LV = left ventricle; NYHA = New York Heart Association; PAF = paroxysmal atrial fibrillation; PM = pacemaker; PsAF = persistent atrial fibrillation; RE-HA = robotic-enhanced hybrid ablation; TIA = transient ischemic attack.

(30%) sets. The optimal cutoff values of individual variables for the best accuracy were determined by the area under the receiver operating characteristic (AUROC) curve analysis, Youden *J* index, and Gini index. The final model was developed using the training dataset and validated on the test dataset using bootstrap with out-of-bag error estimation to yield a robust 95% confidence interval. The DeLong test was used to compare AUROCs. The Hosmer–Lemeshow test was used to assess the goodness-of-fit of the model. All statistical analyses were conducted using R Version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria), with 2-tailed $P < .05$ considered significant.

Results

Baseline characteristics

Characteristics of the study population are summarized in Table 1. Ninety-two patients (age 64 ± 8 years; 66 male [71.7%]; mean body mass index 33 ± 6 kg/m^2) who underwent epicardial RE-HA were included. Median time from AF

Table 2 Overall impedance data and difference between the ineffective and effective RF applications

Variables	All patients (N = 2472)	Ineffective RF application (n = 1722)	Effective RF application (n = 752)	*P* value
Baseline imp	112.27 (44.38)	121.70 (48.99)	90.65 (17.75)	<.001
Imp at 1 s	103.63 (37.43)	110.93 (41.45)	86.91 (16.53)	<.001
Imp at 3 s	99.20 (36.56)	106.29 (40.55)	82.97 (15.93)	<.001
Imp at 5 s	98.16 (36.82)	105.58 (40.75)	81.15 (15.57)	<.001
Imp at 6 s	97.94 (37.03)	105.50 (40.98)	80.20 (15.60)	<.001
Imp at 7 s	98.17 (37.88)	106.02 (41.87)	80.20 (15.60)	<.001
Imp at 8 s	98.39 (38.88)	106.49 (43.04)	79.85 (15.41)	<.001
ID at 1 s	8.63 (13.46)	10.77 (15.57)	3.74 (2.53)	<.001
ID at 3 s	13.06 (13.99)	15.42 (16.04)	7.68 (3.68)	<.001
ID at 5 s	14.11 (14.57)	16.12 (16.85)	9.50 (4.20)	<.001
ID at 6 s	14.33 (14.54)	16.21 (16.84)	10.02 (4.44)	<.001
ID at 7 s	14.10 (15.91)	15.69 (18.63)	10.46 (4.40)	<.001
ID at 8 s	13.87 (17.17)	15.21 (20.20)	10.80 (4.61)	<.001

ID = impedance drop; Imp = impedance; RF = radiofrequency.

diagnosis to the current procedure was 68 [25–85] months, and median CHA_2DS_2-VASc score was 3 [2–5]. Echocardiographic imaging demonstrated mean left ventricular ejection fraction of 55% ± 6% and left atrial volume index of 57 ± 21 mL/m^2. Compared with the LSPAF subgroup, the PsAF subgroup had a significantly shorter median time from diagnosis to the procedure (52 [24–63] months vs 96 [38–105] months, *P* = .003), comparable left atrial volume index (55 ± 19 mL/m^2 vs 61 ± 23 mL/m^2, *P* = .184), and statistically, but not clinically relevant, higher left ventricular ejection fraction (57% ± 7% vs 52% ± 5%, *P* <.001), with a comparable proportion of patients with heart failure with reduced ejection fraction in the LSPAF and PsAF groups (6 [10%] vs 4 [12.5%], *P* = .988).

Procedural outcomes

All patients were in AF during the procedure. Mean duration of epicardial RE-HA, defined as skin-to-skin procedural time, was 132 ± 27 minutes, with no patients requiring conversion to full sternotomy, minithoracotomy, or cardiopulmonary bypass. Median length of hospital stay after the procedure was 3 [2–3.5] days. Major bleedings requiring surgical revision or blood transfusion, operative deaths, stroke, or esophageal injury did not occur. Pleural effusion occurred in 4 patients (4.3%) and required pleural drainage (n = 1) or thoracentesis (n = 3). Hemidiaphragm paralysis was observed in 3 patients (3.2%), with spontaneous resolution within 5 days after the procedure in 2 patients, and only 1 patient requiring thoracoscopic diaphragmatic plication. Additional details are given in Supplemental Table 1.

Biophysical behavior of ablation parameters

A total of 2492 RF applications were performed, with 18 applications excluded because of technical reasons of early (<8 seconds) interruption. Among the 2474 applications (99.3%), there were 752 effective lesions (30.4%) and 1722 ineffective lesions (69.6%).

Mean BI was 112 ± 44 Ω, which is significantly higher in ineffective RF applications than in effective RF applications (122 ± 50 Ω vs 91 ± 18 Ω, *P* <.001).

IDs during the first 8 seconds were significantly lower in effective RF applications compared with ineffective RF applications (*P* <.001), showing a smooth and continuous decrease over time in the effective RF applications (Table 2 and Figure 2). In the inferential analysis (Table 3), parameters associated with effective ablation lesions were BI (odds ratio 0.951, 95% confidence interval [0.945–0.958], *P* <.0001) and ID measurements during the initial seconds of energy application (*P* <.0001 for all). The intraclass correlation coefficients in our study population ranged from 19%–24% (Supplemental Table 2). After variables with variance inflation factor >5 for collinearity were excluded, multivariate logistic regression confirmed BI and ID at 1 and 8 seconds as the most robust independent predictors of effective ablation (*P* <.001). In this composite model, the intraclass correlation coefficient was 27%, implying the presence of mild interpatient variability.

Predictive score

Receiver operating characteristic (ROC) analysis using the Youden *J* index and subsequent validation determined the following optimal cutoff values for predicting effective ablation: <107 Ω [104; 109] for BI, 0–7 Ω for ID at 1 second, and 5–17 Ω for ID at 8 seconds, which achieved AUROC of 0.71 [0.68–0.74], sensitivity 54% [47%–51%], specificity 86% [79%–92%], and accuracy 63% [59%–67%]. These parameters were the strongest predictors of ELRF (Figure 3A). Based on the Youden *J* and Gini indices, the training dataset yielded the following normalized score points (Figure 4): BI ≥107 to ≤125 Ω (1 point) or <107 Ω (2 points); ID at 1 second 0 to <7 Ω (1 point); and ID at 8 seconds 5 to <17 Ω (1 point). The predictive ELRF score ranged from 0–4.

In the test dataset, AUROC of the predictive score was 0.775 [0.747–0.804], with sensitivity 94% [78%–98%], specificity 53% [48%–70%], and accuracy 65% [62%–

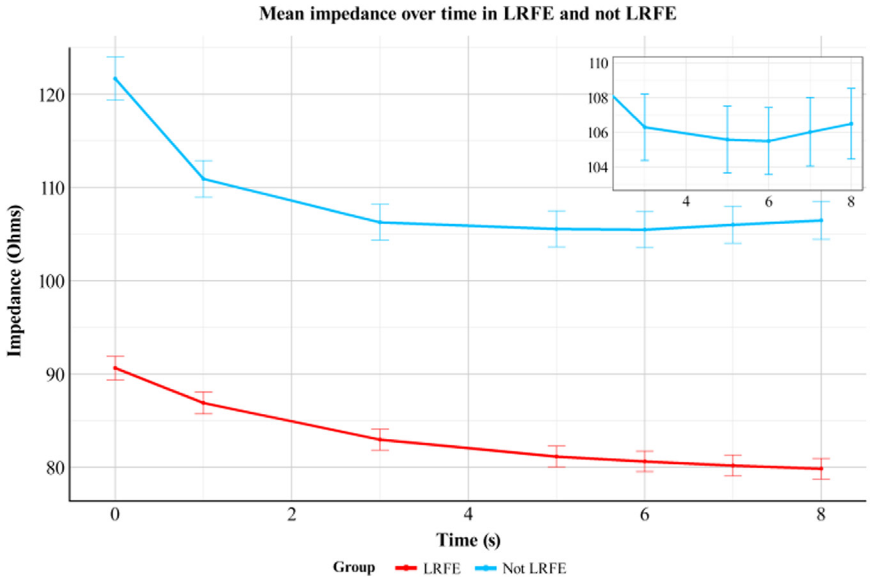

Figure 2 Impedance trend with the first seconds of radiofrequency application. Mean impedance trends during acute effective local epicardial radiofrequency ablation (ELRF) and without ELRF lesions are shown. *Bars* indicate 95% confidence interval limits. **Inset:** Unstable impedance drop (ie, a gradual increase after an initial drop) within the first seconds in the without ELRF lesions.

72%] (Figure 3B). The Youden *J* index identified a cutoff value of 3 points as optimal. The calculated AUROC values were similar between the test and training datasets ($P = .300$) (Figure 5A), indicating a robust predictive model without significant overfitting. Moreover, the Hosmer–Lemeshow test confirmed the absence of significant calibration errors ($P = .125$).

Discussion

To our knowledge, this is the first detailed analysis of the biophysical parameters during epicardial RE-HA in a predictive score model to distinguish between ELRF and no-ELRF lesions. Mean BI was lower in ELRF lesions than in no-ELRF lesions. Early ID was followed by a continuous decrease in impedance during ELRF but not in no-ELRF lesions. Additionally, we observed a relatively mild variance in ID and impedance over time among patients, confirming the hypothesis that the biophysical characteristics of epicardial ablation lesions are reproducible across individuals. Thus, we expect that our novel approach for assessing the effectiveness of epicardial ablation lesions to be applicable in other study populations.

Robotic technology enhances this method by offering enhanced visualization of ablation sites, avoidance of

Table 3 Univariate and multivariate logistic mixed effect model regression analyses

	Univariate analysis*				Multivariate analysis*			
Variables	OR	CI low	CI high	*P* value	OR	CI low	CI high	*P* value
BI	0.951	0.945	0.958	<.0001	0.937	0.927	0.947	<.0001
Imp at 1 s	0.943	0.936	0.951	<.0001	Excluded for collinearity with ID with VIF >10			
Imp at 3 s	0.937	0.928	0.946	<.0001				
Imp at 5 s	0.934	0.925	0.943	<.0001				
Imp at 6 s	0.932	0.923	0.941	<.0001				
Imp at 7 s	0.931	0.922	0.941	<.0001				
Imp at 8 s	0.931	0.922	0.940	<.0001				
ID at 1 s	0.930	0.917	0.944	<.0001	0.965	0.947	0.983	.0001
ID at 3 s	0.934	0.922	0.945	<.0001	Excluded for collinearity with VIF >10			
ID at 5 s	0.955	0.946	0.965	<.0001	Excluded for collinearity with VIF = 5.678			
ID at 6 s	0.959	0.949	0.968	<.0001	Excluded for collinearity with VIF >10			
ID at 7 s	0.976	0.969	0.984	<.0001	Excluded for collinearity with VIF >10			
ID at 8 s	0.985	0.978	0.991	<.0001	0.930	0.909	0.951	<.0001

BI = baseline impedance; ID = impedance drop; Imp = impedance; VIF = variance inflation factor.

*Univariate and multivariate logistic mixed effect model regression analyses were performed after excluding variables for collinearity. The coefficient represented the fixed effect. The odds ratio (OR) with 95% confidence interval (CI) of the impedance variable was calculated.

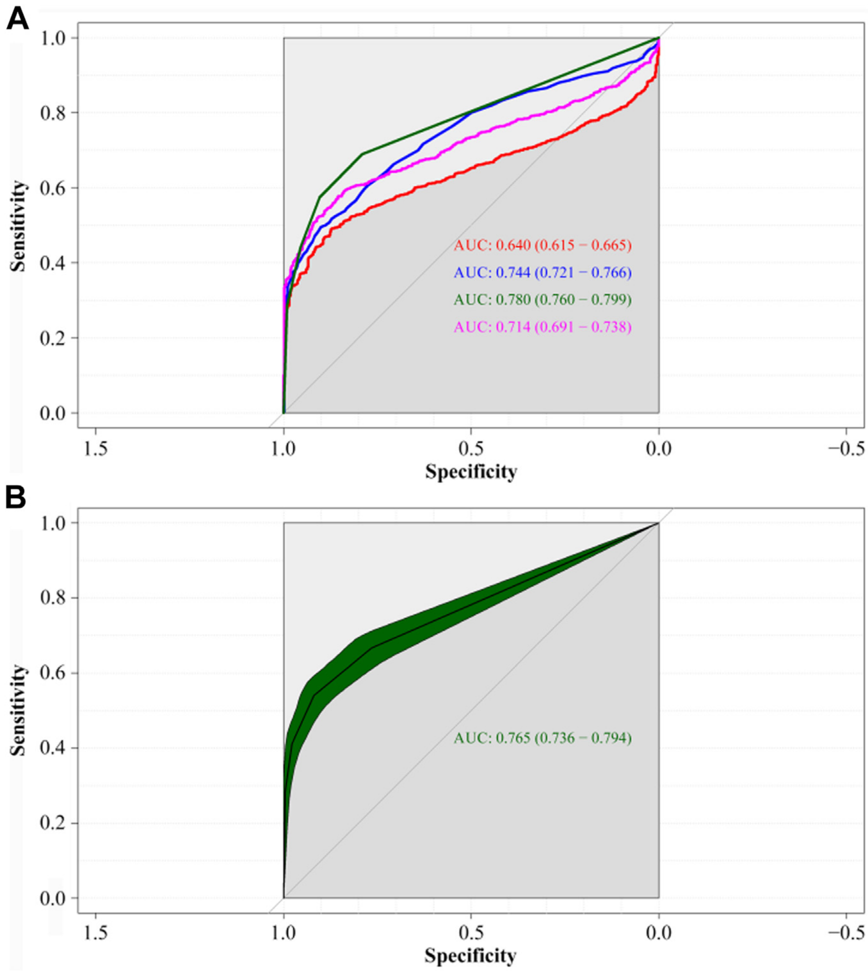

Figure 3 Receiver operating characteristic curve analyses for the single component of the predictive score and the composite score model **(A)** and the validation dataset score **(B).** *Green* indicates the predictive score. *Red* indicates impedance drop (ID) at 8 seconds. *Magenta* indicates ID at 1 second. *Blue* indicates baseline impedance. AUC = area under the receiver operating characteristic curve.

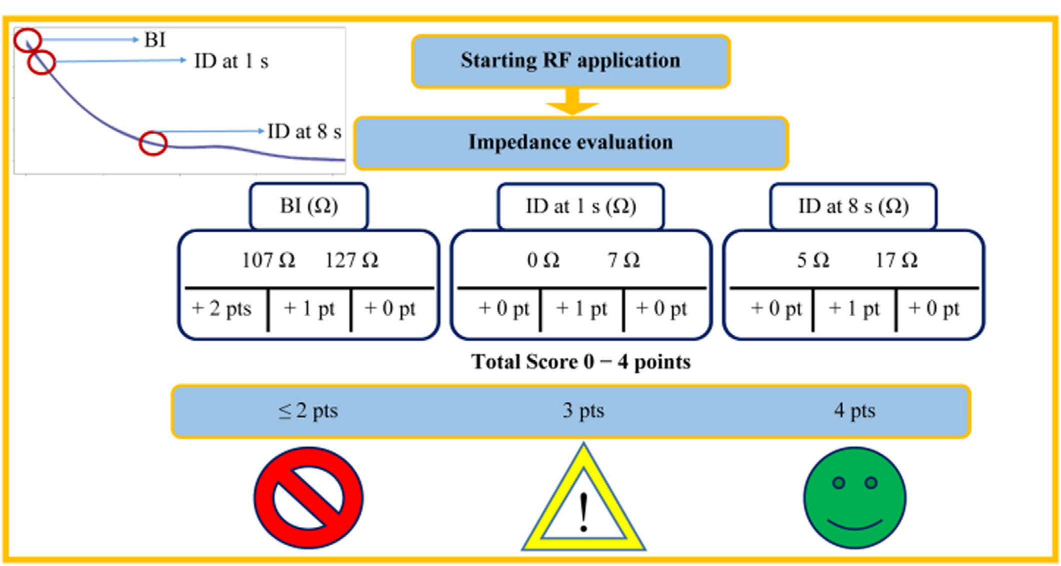

Figure 4 Proposed predictive score for identifying effective local epicardial radiofrequency ablation (ELRF) is analyzed. Analyses of baseline impedance (BI) and impedance drop (ID) at 1 and 8 seconds using the proposed score are shown. The probability of ELRF based on the total score is categorized as follows: 4 = high; 3 = moderate; ≤2 = low. In cases with score ≤2, it is advisable to stop RF application because it has a poor efficacy. RF = radiofrequency.

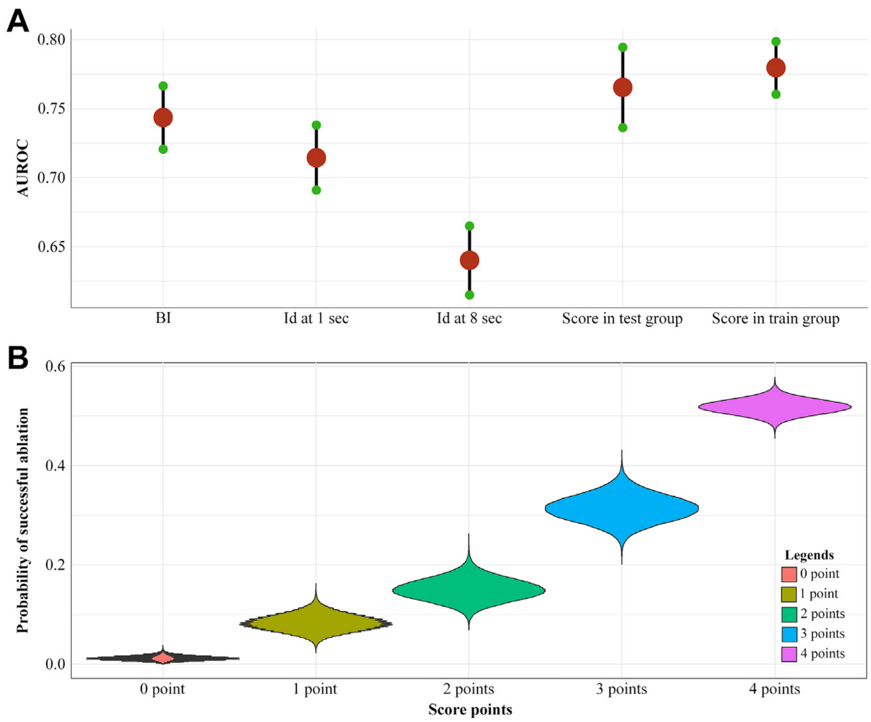

Figure 5 **A:** Bar plot comparing the area under the receiver operating characteristic curve (AUROC) for the single component and composite score models between the training and test groups (*P* value calculated using the DeLong test). **B:** Violin plot displaying the probability of acute effective local epicardial radiofrequency ablation (ELRF) for each score obtained.

epicardial fat tissue, and optimized conduction of RF energy. In our experience, the use of robotic arms has improved ablation probe management, providing greater precision in positioning and increased stability during energy delivery, thereby promoting the creation of fully transmural lesions. Additionally, the unilateral left-sided approach specifically targets the left atrium and left atrial appendage, providing the added benefits of reduced invasiveness and minimized patient morbidity compared to a bilateral approach.[14]

BI

Our findings emphasize that BI is a key predictor of ELRF, which corresponds to previously reported results in an *ex vivo* swine model[18] and "traditional" endocardial RFA.[19–21]

Previous studies have also suggested that epicardial impedance reflects local tissue characteristics, with higher impedance associated with the presence of adipose tissue between the ablation catheter and myocardium.[22] Moreover, the EPi-Sense unipolar probe facilitates blood and air removal, ensuring direct contact between its tip and myocardial tissue. A lack of suction can result in the presence of blood or air layers, which increases BI[23] and reduces energy delivery to the myocardial tissue.

ID

We demonstrated that epicardial ID was a significant independent predictor of ELRF. This finding was previously reported for endocardial RFA[24–26] and was attributed to local temperature elevation and lesion formation. The linear correlation between ID and local temperature has been well documented.[27] Our study highlights the critical role of ID at 1 and 8 seconds. Notably, an abrupt ID within the first second ($>7\ \Omega$) did not reliably predict ELRF and may imply initial heating of blood or serum rather than effective tissue heating. Conversely, an immediate increase in impedance within the first second may suggest inadequate probe–tissue contact. At 8 seconds, sustained and continuous ID was indicative of probe stability and effective energy delivery. Importantly, the absence of collinearity between IDs at 1 and 8 seconds underscored the relevance of maintaining a stable and continuous ID during the initial seconds of ablation to ensure optimal probe performance (Figures 2 and 6). The exclusion of other IDs for collinearity indicated that, in clinical practice, a certain interval before obtaining additional information on the effectiveness of RF application is needed. In this study, the best intervals were identified at 1 and 8 seconds.

Composite predictive model

Based on the results, we developed a predictive score model to distinguish between ELRF and no-ELRF using the 3 most significant variables. A score of at least 3 demonstrated the ability to identify >90% of ELRF lesions, with sensitivity of approximately 94% and negative predictive value of 95%, but average specificity of 53% and positive predictive value of 46% (Figure 5B). This model has the advantage of

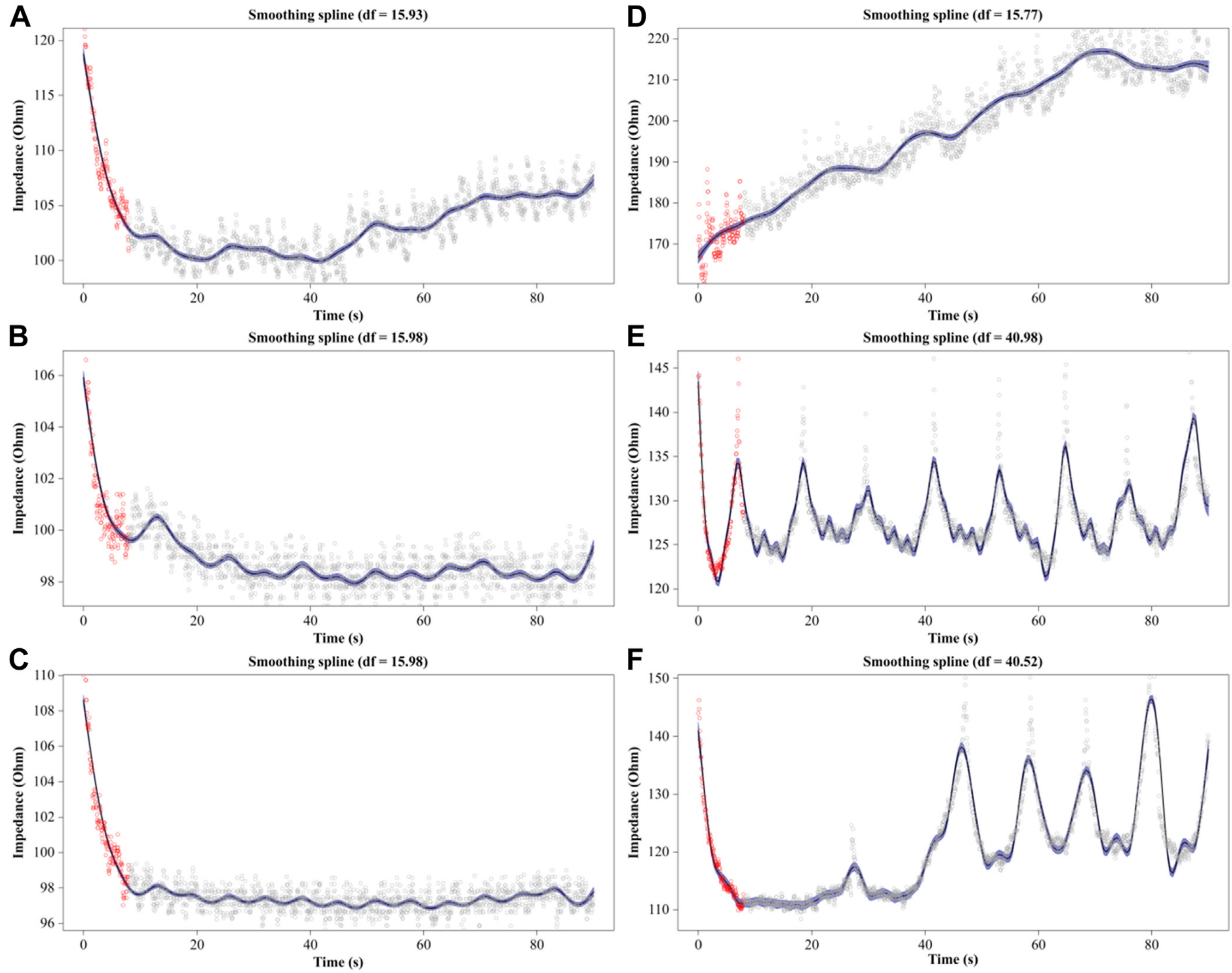

Figure 6 Same examples of impedance profile, in the left side (**A**–**C**) good energy application with LRFE, in the right side (**D**–**F**) not LRFE. LRFE = acute local RF ablation efficacy.

identifying all potential ELRF lesions, thereby allowing the cessation of ineffective applications. However, not all applications with a high predictive score resulted in effective ablation lesion, and observation that may be attributed to probe manipulation. Notably, this composite model outperformed the individual variables in the model (Figure 5A). Use of this predictive score may mitigate complications associated with prolonged anesthesia and RFA, which are more prevalent in patients with PsAF than in those with paroxysmal AF (6.7% vs 3.9%), as highlighted in a recent review by Loring et al.[28]

Study limitations

The retrospective nature of this study may have introduced biases related to population selection and data collection. Furthermore, AtriCure RF generators measure only generator impedance and have limited capabilities to precisely assess local catheter–tissue coupling. This is attributed to modest impedance differences between blood and tissue, as well as significant variations in transthoracic impedance components, including muscle, lung, and bone. Nevertheless, if local impedance is established as the most predictive parameter for lesion formation, particularly in endocardial ablation procedures, generator impedance remains a good surrogate for local impedance.[29] Larger studies are warranted to validate our findings, and prospective application of the composite model in other cohorts would strengthen the value of our results.

Conclusion

BI and continuously progressive and stable ID at 1–8 seconds were the primary predictors of ELRF in RE-HA and significantly enhanced the prediction of effective ablation, with

93% sensitivity and 95% negative predictive value. Early impedance parameters are reliable predictors of acute ELRF in RE-HA. Integration of these parameters into a composite predictive score offers a simple and powerful tool for early identification of ELRF, potentially reducing RF exposure and enhancing procedural speed, effectiveness, and safety. These advances hold promise for improving epicardial RE-HA as an alternative AF therapeutic approach.

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Data Availability: Data will be shared upon reasonable request to the corresponding author.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hroo.2024.11.023.

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