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CLINICAL RESEARCH

Machine learning prediction of outcome following pulsed-field atrial fibrillation ablation: patient selection and risk factors

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Background Despite being the most effective option for maintaining sinus rhythm, atrial fibrillation (AF) catheter ablation reaches few patients. For this reason, identifying candidates with the highest likelihood of success or individualizing counselling to a specific patient to improve procedural outcome could enhance clinical benefits and cost-effectiveness.

Objective To integrate machine learning (ML) into an outcome prediction model based on a large cohort of AF patients undergoing pulsed field ablation (PFA).

Methods Consecutive AF patients undergoing transcatheter PFA between June 2022 and December 2024 were prospectively enrolled in the ATHENA registry. All procedures were performed with a penta-splines 12F over-the-wire PFA catheter (FARAWAVE™, Boston Scientific). Clinical and procedural variables were collected to train five predictive models estimating 1 year arrhythmic recurrence; model interpretability was assessed using SHAP (SHapley Additive exPlanations) analysis.

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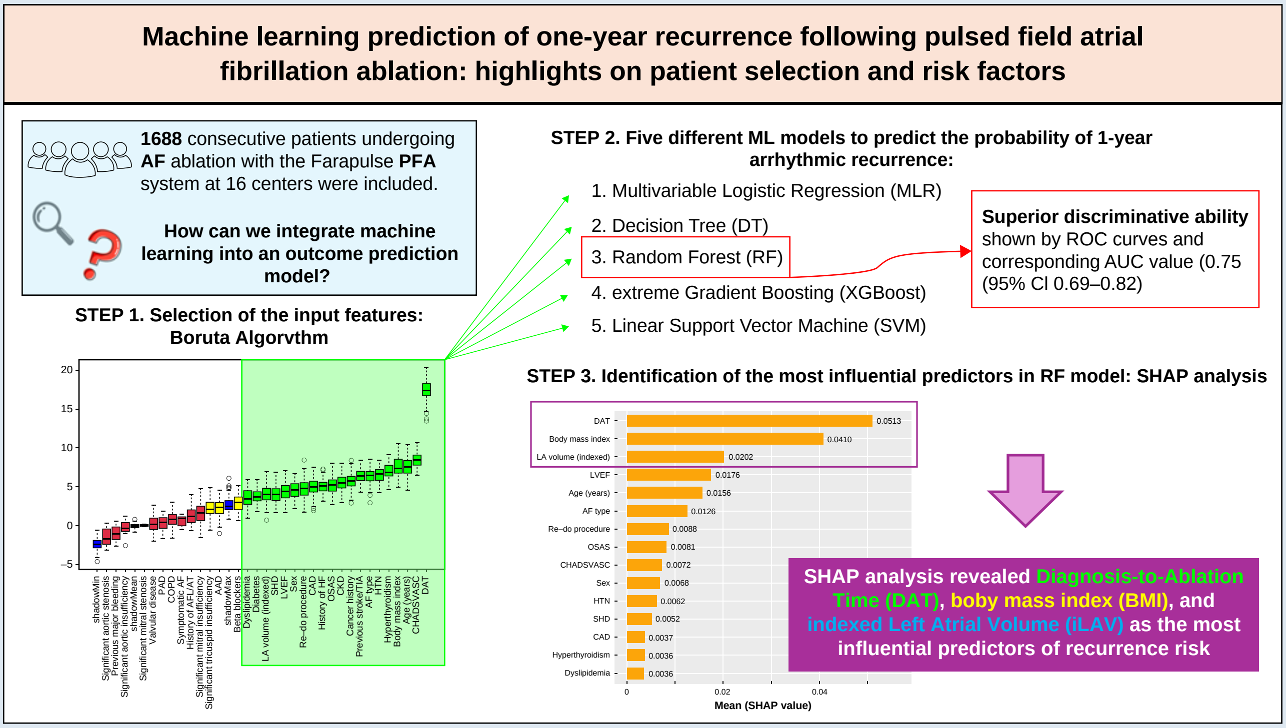
Results The study included 1688 AF patients with a median follow-up of 365 days (interquartile range 202-393), arrhythmic recurrence occurred in 314 patients (18.6%). The Boruta algorithm identified diagnosis-to-ablation time (DAT), CHA_2DS_2-VASc score, age, and body mass index (BMI) as most significant predictors. Among the five ML models developed to predict 1 year arrhythmic recurrence probability, Random Forest achieved the best performance (AUC = 0.75, 95% CI 0.69-0.82). SHAP analysis confirmed DAT, BMI, and indexed left atrial volume as major contributors to recurrence.

Conclusion This is the first ML model exclusively trained and validated on AF patients undergoing PFA providing actionable insights for personalized treatment planning. Routine use of the model holds the potential to optimize patient selection and improve procedural outcome, supporting individualized counselling and outcome-driven care pathways, moving from static to interactive risk prediction.

Clinical Trial Registration Advanced TecHnologies For SuccEssful AblatioN of AF in Clinical Practice (ATHENA). URL: http://clinicaltrials.gov/ Identifier: NCT05617456

Graphical Abstract



Machine learning prediction of one-year recurrence following pulsed field atrial fibrillation ablation: highlights on patient selection and risk factors

1688 consecutive patients undergoing **AF** ablation with the Farapulse **PFA** system at 16 centers were included.

How can we integrate machine learning into an outcome prediction model?

STEP 1. Selection of the input features: Boruta Algorvthm

STEP 2. Five different ML models to predict the probability of 1-year arrhythmic recurrence:

1. Multivariable Logistic Regression (MLR)
2. Decision Tree (DT)
3. Random Forest (RF)
4. extreme Gradient Boosting (XGBoost)
5. Linear Support Vector Machine (SVM)

Superior discriminative ability shown by ROC curves and corresponding AUC value (0.75 (95% CI 0.69–0.82)

STEP 3. Identification of the most influential predictors in RF model: SHAP analysis

SHAP analysis revealed Diagnosis-to-Ablation Time (DAT), boby mass index (BMI), and indexed Left Atrial Volume (iLAV) as the most influential predictors of recurrence risk

Keywords Atrial fibrillation • Electroporation • Pulsed-field ablation • Machine learning • Predictive models • Artificial intelligence

What's new?

Competency of medical knowledge: this study enhances clinicians' ability to identify atrial fibrillation (AF) patients most likely to benefit from pulsed field ablation. By integrating machine learning (ML)-based prediction into clinical decision-making, physicians can improve patient selection, optimize procedural outcomes, and allocate resources more efficiently. Understanding key predictors-such as diagnosis-to-ablation time, body mass index, and indexed left atrial volume-may support more individualized management strategies and promote data-driven, evidence-based care across all stages of professional practice.

Translational outlook: future studies should prospectively validate this predictive model across larger and more heterogeneous populations and evaluate its integration into clinical workflows. Embedding ML algorithms into electronic health records or ablation planning systems could facilitate real-time decision support. Further research incorporating imaging, electrophysiologic, and biomarker data may enhance model precision and advance personalized approaches to AF ablation.

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting over 37 million people globally, with an estimated 4.48 million new cases occurring each year.[1] AF is more prevalent in people with cardiovascular risk factors like hypertension, heart failure (HF), diabetes, and obesity. As populations age, the incidence of AF and its related healthcare burden are projected to increase further.[2]

AF catheter ablation is the most effective method for maintaining sinus rhythm.[3–7] Rather than limiting access based on cost or availability, patient selection should emphasize procedural efficacy and a targeted approach, especially for those with prognostic indications. Modifying risk factors can improve ablation outcomes, and artificial intelligence (AI) may help tailor therapy to individual patient needs.

Current AF ablation outcome scores, such as the APPLE,[8] ALARMEc,[9] and MB-LATER,[10] show moderate predictive performance, with C-statistics typically ranging around 0.60–0.70. These scores use a restricted set of clinical variables and rely on traditional statistical models with limited non-linear capabilities, thus failing to adequately capture the heterogeneity of AF patients and the complex relationships between different variables. In addition, they are further limited by not accounting for variations in ablation techniques and energy sources [e.g. radiofrequency, cryoablation, pulsed-field ablation (PFA)]. As a result, their performance in predicting real-world ablation outcomes and their utility in personalized decision-making remains limited.

AI and machine learning (ML) approaches have strong potential to improve AF ablation outcome prediction by addressing the limitations of current clinical scoring systems.[11] By integrating multimodal inputs, ML can identify complex patterns in a highly non-linear fashion and provide personalized, data-driven risk assessments. This enables more accurate and individualized predictions of ablation success, not to exclude patients from

Table 1 Baseline characteristics of the included patients, also stratified by the occurrence of the study outcome

Variable	**Overall**	**No**	**Yes**	***P***	**Missing (%)**
n	**1688**	**1374**	**314**		
Age (years) [mean (SD)]	62.61 (9.55)	62.56 (9.49)	62.82 (9.82)	0.670	4
Sex = female (%)	446 (26.4)	349 (25.4)	97 (30.9)	0.055	5
Body mass index [mean (SD)]	27.07 (3.78)	26.97 (3.65)	27.54 (4.29)	0.016	30
AF type = persistent (%)	524 (31.0)	410 (29.8)	114 (36.3)	0.030	1
Symptomatic AF = symptomatic (%)	1340 (79.4)	1093 (79.5)	247 (78.7)	0.785	0
History of AFL/AT = yes (%)	283 (16.8)	225 (16.4)	58 (18.5)	0.416	0
SHD = yes (%)	459 (27.2)	359 (26.1)	100 (31.8)	0.047	20
CAD = yes (%)	421 (24.9)	334 (24.3)	87 (27.7)	0.237	22
PAD = yes (%)	44 (2.6)	37 (2.7)	7 (2.2)	0.788	27
Valvular disease = yes (%)	75 (4.4)	61 (4.4)	14 (4.5)	1.000	23
Moderate-to-severe aortic stenosis = 1 (%)	2 (0.1)	1 (0.1)	1 (0.3)	0.816	30
Moderate-to-severe aortic insufficiency = 1 (%)	23 (1.4)	18 (1.3)	5 (1.6)	0.905	29
Moderate-to-severe mitral insufficiency = 1 (%)	129 (7.6)	100 (7.3)	29 (9.2)	0.289	27
Moderate-to-severe mitral stenosis = 1 (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA	30
History of HF = yes (%)	286 (16.9)	229 (16.7)	57 (18.2)	0.582	23
CKD = yes (%)	203 (12.0)	167 (12.2)	36 (11.5)	0.808	24
COPD = yes (%)	46 (2.7)	36 (2.6)	10 (3.2)	0.717	26
Previous stroke/TIA = yes (%)	210 (12.4)	170 (12.4)	40 (12.7)	0.934	24
Hyperthyroidism = yes (%)	217 (12.9)	174 (12.7)	43 (13.7)	0.690	25
Cancer history = yes (%)	248 (14.7)	198 (14.4)	50 (15.9)	0.552	25
OSAS = yes (%)	213 (12.6)	168 (12.2)	45 (14.3)	0.358	20
Diabetes = yes (%)	354 (21.0)	288 (21.0)	66 (21.0)	1.000	18
HTN = yes (%)	941 (55.7)	754 (54.9)	187 (59.6)	0.149	12
Dyslipidaemia = yes (%)	648 (38.4)	516 (37.6)	132 (42.0)	0.159	13
Previous major bleeding = 1 (%)	11 (0.7)	9 (0.7)	2 (0.6)	1.000	20
AAD = yes (%)	1035 (61.3)	838 (61.0)	197 (62.7)	0.610	16
Beta blockers = yes (%)	1028 (60.9)	822 (59.8)	206 (65.6)	0.067	16
Re-do procedure = yes (%)	253 (15.0)	180 (13.1)	73 (23.2)	<0.001	4
Significant tricuspid insufficiency = 1 (%)	62 (3.7)	47 (3.4)	15 (4.8)	0.324	28
DAT [mean (SD)]	1469.58 (1636.51)	1377.30 (1604.59)	1873.35 (1714.53)	<0.001	23
LA volume (indexed) [mean (SD)]	38.49 (10.45)	38.32 (10.44)	39.25 (10.50)	0.152	30
LVEF [mean (SD)]	57.98 (7.34)	58.04 (7.18)	57.72 (8.00)	0.485	24
CHADSVASC [mean (SD)]	1.78 (0.96)	1.76 (0.97)	1.89 (0.92)	0.030	23

referral to ablation but to better tailor procedural approaches, guide risk factor modification, and support informed shared decision-making, offering a major advancement over traditional models.[12]

The aim of this study is to integrate AI into an outcome prediction model based on a large cohort of AF patients undergoing pentaspline PFA, a novel, standardized, tissue-selective, and safer technique for AF ablation.[13,14]

Methods

Patient population

Consecutive patients with AF referred for transcatheter ablation were prospectively enrolled between June 2022 and December 2024 in the Advanced TecHnologies For SuccEssful AblatioN of AF in Clinical Practice (ATHENA) at 16 Italian centres (Clinical Trial Registration at http://clinicaltrials.gov, Identifier: NCT05617456), with a median number of patients per centre of 63.5 (interquartile range, IQR: 30–169). Despite the fact that inclusion period spans early and later phases of adoption, given for this technology, multiple studies and registry data have consistently shown that the learning curve is very rapid and does not significantly affect procedural outcomes or the reproducibility of the technique[15]; a meaningful impact of operator or centre-level learning effects on the reported outcomes is unlikely. All patients were followed at the enrolling centre, from the time of first ablation to the last follow-up visit. The study complied with the Declaration of Helsinki; the locally appointed ethics committee approved the research protocol, and informed consent was obtained from all patients before the ablation procedure.

Ablation procedure

All procedures were performed under either deep conscious sedation or general anaesthesia. The choice of anaesthesia protocol was guided by the operator's preference, expertise, and the patient's overall health status. Anticoagulation was administered in adherence to available guidelines.[5,16] After the transseptal puncture, procedural activated clotting times were maintained at a minimum of 300 s through the administration of intravenous heparin bolus or continuous infusion. The procedures were performed with a penta-splines 12F over-the-wire PFA catheter (FARAWAVE™, Boston Scientific). Pulmonary vein isolation (PVI) was performed by means of four applications in a basket configuration and four applications in a flower configuration per pulmonary vein, as described elsewhere.[17] Between pairs of PFA applications, the catheter was rotated by about 30/45° after the first two applications in each configuration, to cover the entire vein's circumference. Ablation was performed by using an amplitude setting of 2.0 kV for each of the four PVs. Additional lesions at any pulmonary vein or beyond (e.g. posterior wall) were deployed per physician's discretion.

Post-ablation management

Follow-up evaluations were conducted at outpatient clinics at 1, 3, 6, and 12 months post-procedure or as needed in response to patient complaints. These assessments comprised a detailed review of medical history, physical examination, 12-lead electrocardiography, Holter monitoring (24 h, 48 h, or 7 days), and evaluation for adverse events. Anticoagulation and antiarrhythmic therapies were maintained following the ablation. At the 3 month follow-up, decisions regarding the continuation of anticoagulation therapy were guided by the patient's stroke risk, while the ongoing use of antiarrhythmic drugs (AAD) was determined at the treating physician's discretion. During the initial 3 month period post-ablation (the blanking period), occurrences of AF or atrial tachycardia (AT) were not classified as recurrences.

Machine learning framework

In the present study, the development, training, validation, and reporting of AI models were conducted in accordance with the EHRA AI checklist.[18] The completed checklist is reported in the Supplementary Material (Supplementary material online, *Table S1*).

Outcome of interest

The primary outcome was arrhythmia recurrence, defined as any electrocardiographically documented episode of AF, atrial flutter (AFL), or AT lasting ≥30 s, occurring after the blanking period and within the first post-procedural year.

Variable selection and feature engineering

We have conformed to the suggested guidelines for a structured framework for reporting AI research in EP.[14] A comprehensive set of candidate variables was collected for each patient, with the aim of including parameters routinely available in standard clinical practice. Variable selection was initially guided by clinical reasoning, focusing on clinically meaningful and easily accessible features. Specifically, the following variables were considered as candidates for model development: age, sex, AF type (paroxysmal/persistent), symptomatic AF, diagnosis-to-ablation time (DAT), history of AFL/AT, indexed LA volume, moderate-to-severe aortic stenosis, moderate-to-severe aortic insufficiency, moderate-to-severe mitral insufficiency, moderate-to-severe mitral stenosis, moderate-to-severe tricuspid insufficiency, structural heart disease (SHD), coronary artery disease (CAD), peripheral arterial disease (PAD), valvular disease, history of HF, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), previous stroke/transient ischaemic attach (TIA), hyperthyroidism, cancer history, body mass index, obstructive sleep apnoea syndrome (OSAS), diabetes, hypertension (HTN), dyslipidaemia, previous major bleeding, CHA_2DS_2–VASc score, AAD, beta blockers, and re-do procedure.

Missing data imputation was performed only after confirming that all selected variables had a missing rate of maximum 30%. Remaining missing values were imputed using a k-nearest neighbours (kNN) algorithm ($k = 5$), implemented through the *VIM* R package, based on all candidate predictors and using the Euclidean distance as the default metric. Continuous variables were imputed using the mean of the kNN, while categorical variables were imputed using the most frequent category. The extent of missing data for each variable prior to imputation is reported in *Table 1* as the percentage of missing observations.

Baseline characteristics were summarized according to the variable type. Continuous variables were reported as mean ± standard deviation, whereas categorical variables were expressed as absolute counts and percentages. These descriptive statistics were also stratified by the outcome of interest, providing a comparative overview of patients with and without 1 year arrhythmic recurrence. Between-group comparisons were performed using the *t*-test for continuous variables and the χ^2 test for categorical variables.

Feature selection for subsequent ML models was then carried out using the Boruta algorithm, a random forest–based wrapper method that iteratively compares the importance of actual features with that of randomly permuted 'shadow' features. This approach enabled the identification and retention of variables with statistically significant relevance for model training.

Feature selection was performed using the Boruta algorithm, a wrapper-based method that iteratively compares the importance of original features with that of randomly permuted 'shadow' features, allowing the identification of variables carrying statistically significant predictive information.

Machine learning models

Five predictive models were developed to estimate the probability of 1 year arrhythmic recurrence, including:

(1) Multivariable Logistic Regression (MLR)
(2) Decision Tree (DT)
(3) Random Forest (RF)
(4) eXtreme Gradient Boosting (XGBoost)
(5) Linear Support Vector Machine (SVM)

All models were trained using features selected by the Boruta algorithm, ensuring that only variables with significant predictive value were included while maintaining a consistent feature set across classifiers to allow fair performance comparison and improve model stability.

Model training and validation

The dataset was randomly partitioned at the procedure level into training (80%) and testing (20%) subsets, using outcome-stratified sampling. Model development and hyperparameter optimization were conducted exclusively on the training set using a grid search approach with 10-fold cross-validation, while the test set was reserved for final performance evaluation. All models were implemented using the caret package in R (version 4.0.0, R Foundation for Statistical Computing, Vienna, Austria; available at https://cran.r-project.org/web/packages/caret/caret.pdf).

Performance evaluation and final model selection

Model performance was assessed on the test set using the area under the receiver operating characteristic curve (AUC) as the primary metric. AUC values were compared across models, and the model with the highest AUC was chosen as the final classifier. This metric was selected for its ability to evaluate the model's discriminative capacity between patients with and without 1 year arrhythmic recurrence, independent of specific classification thresholds, providing a robust measure of predictive performance. Ninety-five per cent confidence intervals for the AUC were calculated using the DeLong method.

Evaluation of model calibration

Additional analyses were performed to assess performance beyond overall discrimination. Calibration of the final model was evaluated using the Hosmer–Lemeshow goodness-of-fit test to determine the agreement between predicted probabilities and observed

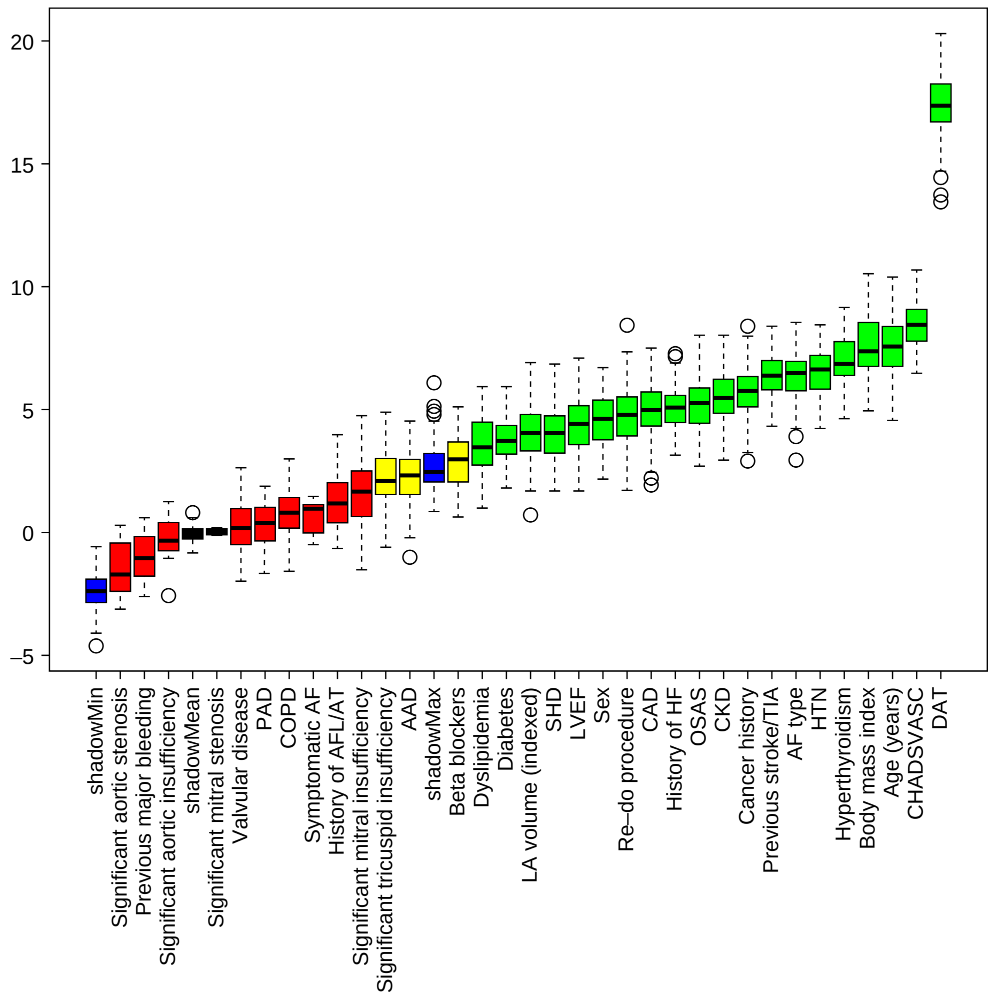


Figure 1 Feature importance from Boruta selection. This plot illustrates the importance scores of features assessed by the Boruta algorithm. Green indicates confirmed important variables, red denotes rejected ones, and yellow represents tentative variables. The x-axis lists feature names, and the y-axis shows the Z-scores of importance. Only confirmed important variables were retained as input features for the subsequent training of ML models.

arrhythmic recurrence outcomes, as well as by estimating the calibration intercept and slope with 95% confidence intervals and the Brier score on the independent test set, providing a comprehensive assessment of model calibration and overall probabilistic accuracy. In addition, calibration metrics were systematically evaluated across all investigated classifiers, to enable a comparative assessment of calibration performance. Finally, a detailed Receiver Operating Characteristic (ROC) analysis was conducted on the final model to identify the optimal classification threshold using the Youden index, which optimizes the balance between sensitivity and specificity. Additionally, sensitivity and specificity were calculated at probability thresholds corresponding to the tertiles of predicted probabilities in the test set.

Model explainability and variable effect analysis

To enhance the clinical interpretability of the best-performing model, SHAP (SHapley Additive exPlanations) analysis was applied. This method provided insights into global feature importance and local, patient-specific contributions to predictions, enabling transparent and clinically relevant interpretations of the model's decision-making process. In addition, partial dependence plots (PDP) and individual conditional expectation (ICE) plots for the most relevant features identified at the SHAP analysis were generated. PDP illustrate the average effect of a specific feature on the model's predictions while marginalizing over the values of all other features. By averaging the model's output across the dataset for different values of a selected variable, PDPs provide a global view of how changes in that variable influence the predicted outcome, assuming all other variables remain constant. ICE plots, in contrast, disaggregate this relationship by displaying the model's predicted response for each individual patient as the value of a single feature is varied. ICE plots reveal heterogeneity in the effect of a variable across patients, highlighting potential non-linear or patient-specific patterns that may be obscured in PDPs. Both PDP and ICE plots were constructed for key features identified by the SHAP analysis, permitting complementary insights into the global and individual-level contributions of variables to the model's predictions. These visualizations facilitate a deeper understanding of the model's behaviour and support its clinical applicability by elucidating the impact of individual predictors.

Online calculator

To facilitate the clinical applicability of the proposed model, an online calculator was developed to estimate the individual probability of the study outcome based on patient-specific characteristics. The calculator implements the final selected model and allows users to input the required clinical variables to obtain a predicted probability

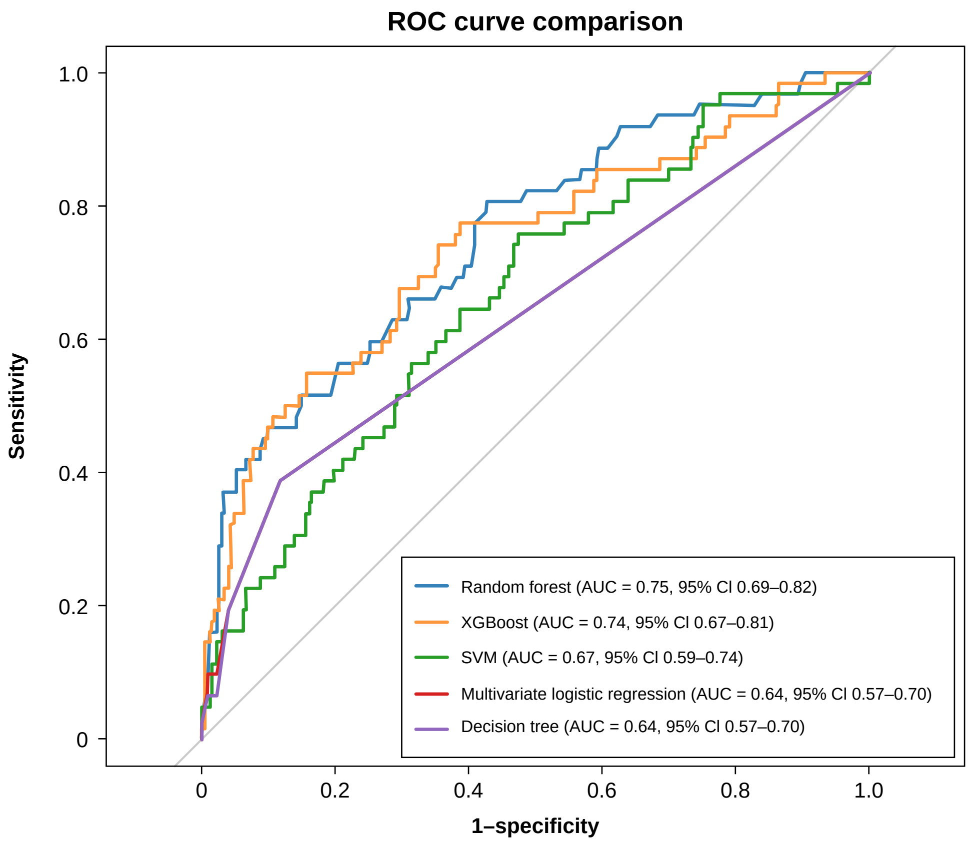


Figure 2 ROC curve comparison of ML models for predicting 1 year arrhythmic recurrence after AF catheter ablation on the test set.

in real time. The tool is freely accessible at the following link: https://asaglietto.shinyapps.io/PFA_ML/.

Results

Patient population

In this investigation a cohort of 1688 AF patients referred for PFA ablation were followed for a median follow-up duration of 365 days (IQR 202–393 days). The baseline characteristics of the entire study population, as detailed in *Table 1*, indicated a mean age of 62.6 ± 9.6 years, with 26.4% being female. Thirty-one per cent of the patients presented persistent AF, while 69.0% had paroxysmal AF. Overall, AF was symptomatic in 79.4% of the cases. A history of AFL/AT was noted in 16.8% of patients but was never the main indication for the procedure. Structural heart disease (SHD) was present in 27.2% of the population, and CAD was identified in 24.9%. History of HF was observed in 16.9% and previous major bleeding occurred in 0.7%. The mean indexed left atrial volume was 38.5 ± 10.5 mL/m^2, while mean body mass index and CHA$_2$DS$_2$–VASc score were, respectively, 27.1 ± 3.8 kg/m^2 and 1.8 ± 1.0. Concerning pre-procedural pharmacological treatment, 61.3% were on AAD, while 60.9% used beta blockers. The mean DAT was 1469 ± 1.636 days. Re-do procedures accounted for a minority of the cases (15%). PVI-only was performed in 72.7% of patients, while additional lesion sets at sites beyond the pulmonary veins were applied in 27.3% of cases, at the discretion of the treating physician. These additional lesions predominantly involved the left atrial posterior wall (25.9%), which was isolated as the sole extra target in 20.8%, combined with a roof line in 4.8% and with other targeted sites in 0.3% of the cases, respectively. Ablation at non–posterior wall locations was performed in 1.4% of cases, mainly consisting of a roof line alone. The median number of PFA applications was 33 (IQR 32–46) at the pulmonary veins and 16 (IQR 12–22) at sites beyond the pulmonary veins, resulting in a total median of 40 (IQR 32–48) applications. The procedure was performed under general anaesthesia in 81.1% of the cases. Periprocedural complications occurred in 17 cases (1.0%), including 9 (0.5%) vascular complications, 5 (0.3%) pericardial effusions/tamponade, 1 (0.06%) transient ischaemic attack, and 1 (0.06%) post-procedural infection.

Overall, any arrhythmic recurrence was documented in 314 patients (18.6%). In particular, AF was documented in 236 patients (14.0%), while AT/AFL was documented in 102 patients (6%). *Table 1* provides baseline clinical characteristics also stratified by the primary outcome (1 year arrhythmic recurrence vs. no recurrence). The predictive performance of the APPLE score, the most widely used traditional statistical risk score for predicting arrhythmic recurrence after ablation, applied to the subset of patients for whom all required variables were available, was poor (AUC 0.514, 95% CI 0.393–0.636).

Feature selection

Feature selection was conducted using the Boruta algorithm to determine the most influential variables for predicting 1 year arrhythmic recurrence. As depicted in *Figure 1*, the majority of

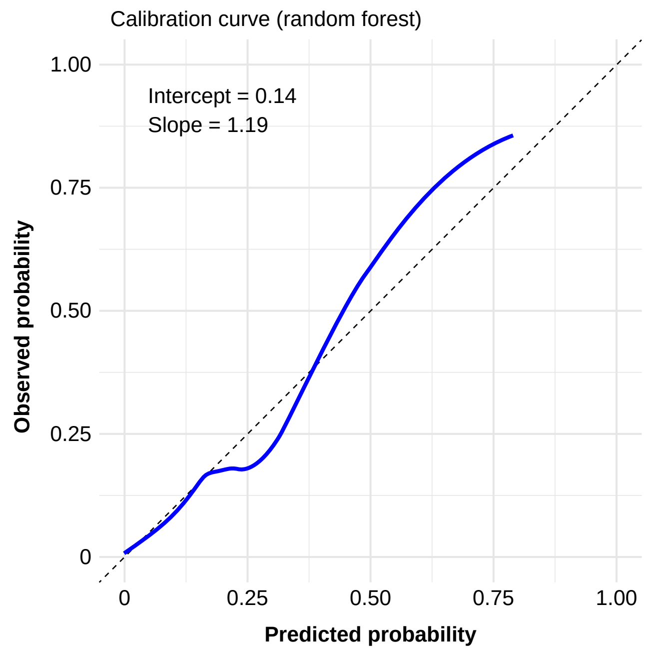


Figure 3 Calibration plot. The plot shows predicted probabilities vs. observed outcome frequencies, with the solid line representing the smoothed calibration curve and the dashed line indicating ideal calibration. The random forest model demonstrates good agreement between predicted and observed risks across the range of predicted probabilities, consistent with a calibration intercept close to zero and a calibration slope close to one.

Table 2 Threshold analysis

Threshold type	Threshold value	Sensitivity	Specificity
33.33%	0.116	0.903	0.379
Youden	0.163	0.806	0.572
66.67%	0.218	0.613	0.722

The optimal cut-off was determined using the Youden index, with sensitivity and specificity values also reported for the tertiles of predicted probabilities on the test set.

features, with the exception of significant aortic stenosis, were identified as significant and included in the subsequent modelling process. Among these, DAT, CHA_2DS_2–VASc score, age, and BMI emerged with the highest importance scores, underscoring their substantial impact on the model’s predictive capability.

Machine learning models

Subsequently, five ML models (MLR, DT, RF, XGBoost, and SVM) were developed to predict the probability of 1 year arrhythmic recurrence using the input features derived from the Boruta algorithm selection. Model performance during training was assessed using 10-fold cross-validation, and detailed distributions of ROC AUC values across resamples for each model are reported in the Supplementary Material (Supplementary material online, *Table S2*). Across cross-validation folds, RF and XGBoost models demonstrated the highest and most consistent discriminative performance, with mean AUC values of 0.73 and 0.72, respectively. On the test set, the RF model achieved the highest AUC of 0.75 (95% CI 0.69–0.82), leading to its selection as the final classifier. A comparison of ROC curves with corresponding AUC values and 95% CI for all models is presented in *Figure 2*, emphasizing the superior discriminative ability of the RF model.

Calibration, threshold analysis, and explainability of the best-performing model

RF model calibration was evaluated on the test set, showing good alignment between predicted and observed probabilities (*P*-value of Hosmer–Lemeshow test: 0.101).The calibration curve plotting predicted vs. observed probabilities for RF model is reported in *Figure 3* to visually illustrate model calibration. The calibration intercept was 0.14 (95% CI −0.38 to 0.69), and the calibration slope was 1.19 (95% CI 0.83–1.59), indicating good agreement between predicted and observed risks. The Brier score was 0.125, supporting good overall probabilistic accuracy. Together with the graphical calibration assessment, these findings suggest adequate calibration of the proposed model. Among all evaluated classifiers, RF model demonstrated the most favourable calibration profile, as reported in Supplementary material online, *Table S3*.

The threshold analysis of the RF model identified an optimal cut-off of 0.163 based on the Youden index, yielding a sensitivity of 81% and a specificity of 57%, reflecting a balanced performance in predicting 1 year arrhythmic recurrence (*Table 2*). Further evaluation at the tertiles of predicted probabilities revealed a sensitivity of 90% and a specificity of 38% at the 33.3% threshold (0.116) and a sensitivity of 61% with a specificity of 72% at the 66.7% threshold (0.218).

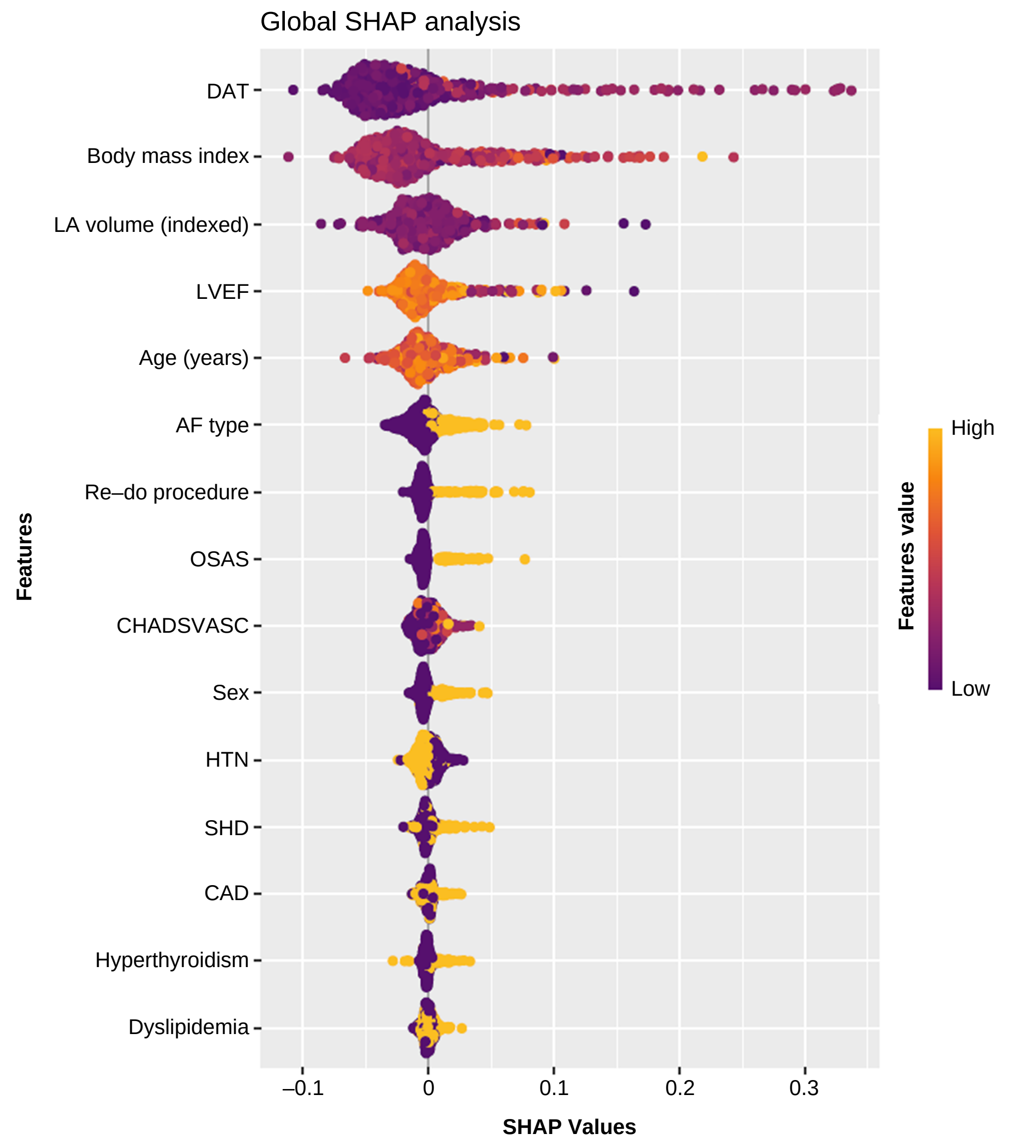


Figure 4 Global SHAP analysis. This figure displays the overall significance of features and their collective influence on predicting 1 year arrhythmic recurrence. The colour gradient (yellow to purple) reflects the range from high to low feature values, while the SHAP values highlighting the direction and extent of each feature's contribution to the model's predictions (positive values indicate higher predicted 1 year arrhythmic recurrence risk, whereas negative values indicate lower predicted risk).

The SHAP analysis provided a comprehensive understanding of feature importance and patient-specific interpretability for the top-performing RF model. Globally, the analysis (*Figure 4*) highlighted the overall influence of various features on the prediction of 1 year arrhythmic recurrence, with DAT, body mass index (BMI), and indexed left atrial volume (LA volume) emerging as the most significant contributors. Longer DAT values were associated with an increased likelihood of recurrence, while higher BMI and greater LA volume tended to elevate the recurrence risk, as indicated by the SHAP values and their directional impact. For individualized insights, the SHAP analysis presented in *Figure 5* featured waterfall plots for two patients—one with recurrence and one without—highlighting the distinct impact of features on the predicted outcome and facilitating personalized clinical interpretations. Additionally, the PDP and ICE plots (see Supplementary material online, *Figure S1*) for these three key variables illustrated the average trend (red PDP line) and patient-specific variations (black ICE lines), providing a detailed view of how these factors shape recurrence risk across the test set.

Discussion

Main study findings

To the best of our knowledge, this study describes the first ML model exclusively trained and validated on a cohort of AF patients undergoing PFA, a novel, standardized, tissue-selective, and safer ablation technique. The model aims to identify patients most likely to benefit from PFA, optimizing clinical

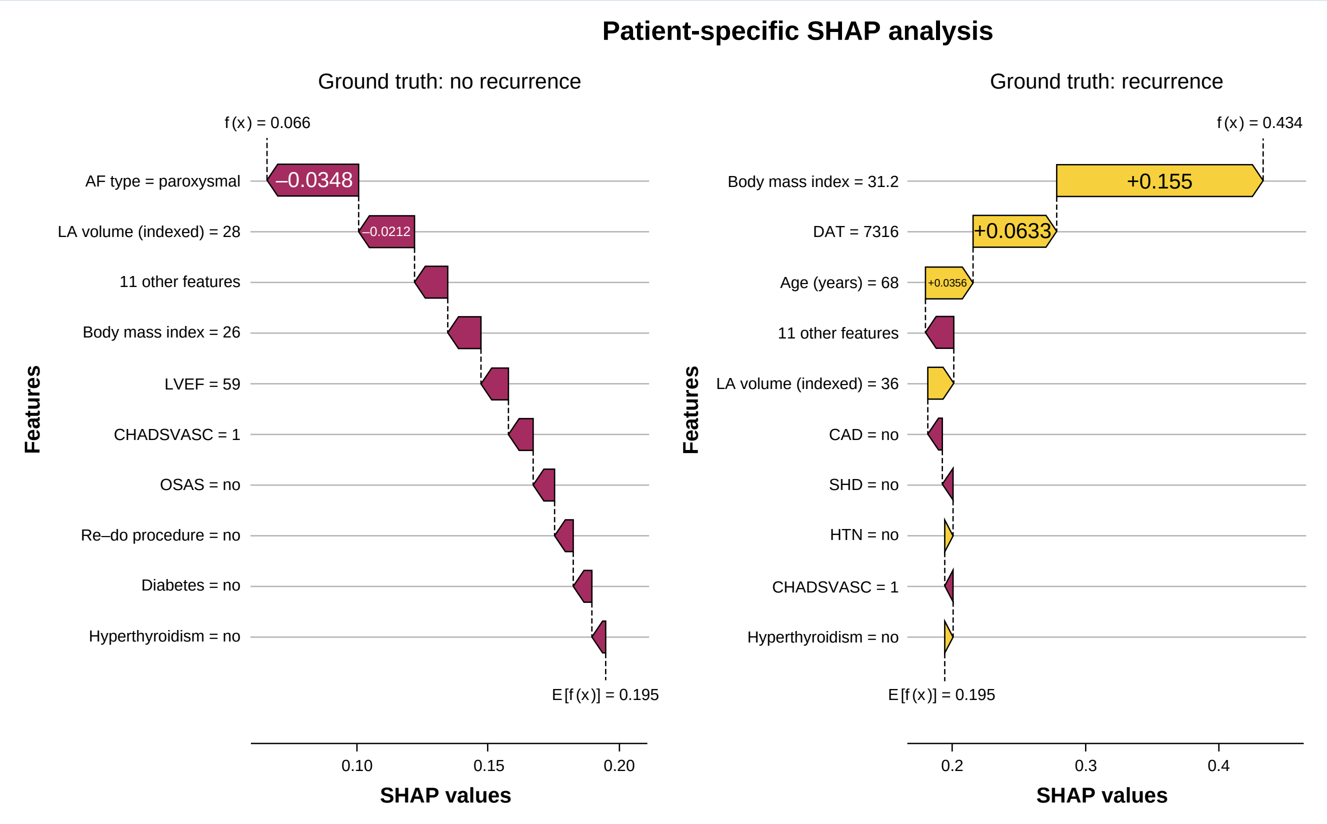


Figure 5 Patient-specific SHAP analysis. This figure showcases two waterfall plots of SHAP values for individual patients, one with 1 year arrhythmic recurrence (left) and one without (right), providing insight into the personalized impact of features on the predicted outcome. Positive SHAP values push the prediction towards higher risk, and negative values push the prediction towards lower risk.

outcomes and resource allocation, while highlighting modifiable factors that influence procedural success, empowering patients and clinicians to take proactive steps towards improved results. The main findings of the present study are:

- This multicentre study introduces a ML random forest model to predict 1 year arrhythmic recurrence in 1688 AF patients undergoing PFA, achieving an AUC of 0.75 (95% CI 0.69–0.82) and demonstrating good predictive performance.
- Global SHAP analysis identifies DAT, BMI, and indexed LA volume as the most influential predictors, with longer DAT, higher BMI, and larger LA volume linked to increased recurrence risk.
- SHAP-driven patient-specific interpretability of RF model output, as well as PDP and ICE plots, enhance personalized risk assessment, guiding tailored clinical decisions in PFA to optimize patient outcomes.

Pitfalls of clinical risk scores based on classical statistical approach

Current clinical risk scores for predicting AF recurrence after catheter ablation, such as the APPLE, ALARMEc, and MB-LATER scores,[19–21] rely on classical statistical methods that utilize weighted sums of a limited set of clinical variables, such as left atrial parameters, type of AF, and age. These models assume linear relationships between variables and outcomes, inherently overlooking the complex, non-linear interactions and heterogeneity that characterize the atrial cardiomyopathy at the base of arrhythmia progression.[22] The AF population is highly heterogeneous, and recurrence reflects multiple mechanisms (trigger- vs. substrate-driven disease, procedural differences), so important risk signal can arise from non-linear effects and interactions among common clinical factors. A systematic review of prognostic models based on classical statistical methods for AF recurrence post-ablation[19] highlights, in fact, significant limitations in their performance, with AUCs typically ranging from 0.60 to 0.70, indicating suboptimal discriminatory ability, consistent with incomplete capture of heterogeneity and limited generalizability. Moreover, the review underlines that model performance is highly variable across studies, with no single model consistently demonstrating poor or good performance. Another critical shortcoming of these traditional models is the frequent lack of calibration assessment, which is essential for evaluating how well predicted probabilities align with observed outcomes. The same systematic review found that most studies developing or validating these scores did not report calibration metrics, raising concerns about their reliability in clinical practice. Without proper calibration, these models risk providing misleading risk estimates, potentially leading to suboptimal patient management decisions. Additionally, the reliance on a small number of pre-selected variables limits their ability to account for the full spectrum of different factors contributing to AF recurrence, further diminishing their predictive power.

ML-based scoring system

In contrast, ML approaches provide a transformative solution by leveraging advanced computational techniques to model intricate, non-linear relationships across diverse feature sets. In the context of prediction of AF recurrence after catheter ablation, a pivotal example of this is the AFA-Recur model,[12] previously developed by our group based on the ESC-EHRA Atrial Fibrillation Ablation Long-Term Registry, which utilizes readily available clinical and echocardiographic variables, such as left atrial size, AF type, and patient demographics, to predict AF recurrence post-ablation. Employing supervised ML algorithms, including random forests and gradient boosting, AFA-Recur achieved an AUC of 0.72 on the testing cohort, markedly outperforming a traditional score like APPLE score (AUC 0.55). In addition, different ML approaches have further advanced AF outcome prediction by incorporating complex multimodal data from advanced imaging, such as computed tomography (CT). For instance, Yang *et al.*[23] developed an ML-based radiomics model using CT-derived features of epicardial adipose tissue around the left atrium (LA-EAT), combined with clinical variables, to predict AF recurrence post-ablation. Their model achieved an AUC of 0.79 in the validation cohort, demonstrating improved predictive accuracy over traditional models. Similarly, Atta-Fosu *et al.*[24] utilized CT-based imaging data to develop an ML model for predicting AF recurrence, integrating radiomic features with clinical and procedural variables, achieving enhanced performance over classical scores. These studies highlight the potential of advanced imaging to improve AUCs beyond those of models reliant on clinical data. However, such approaches entail significant trade-offs, including increased data acquisition complexity, reduced cost-effectiveness, and limited scalability due to the need for specialized imaging equipment and expertise. Compared with AFA-Recur, which simply relies on solely pre-procedural and widely available clinical and echocardiographic data, these imaging-based models might be less feasible for widespread clinical adoption, posing challenges in accessibility and resource allocation. Reliance on a limited variable set can be a limitation when it represents an incomplete phenotype; however, using easily available variables supports implementation in routine clinical practice, anyhow enabling capture of non-linearities and complex interactions within these standard features. In this context, the added value of the proposed ML approach lies primarily in its ability to integrate such routinely collected variables in a non-linear and interaction-aware manner, rather than in the identification of novel predictors *per se*. Nevertheless, future studies incorporating a broader range of more complex features may further enhance model performance and better exploit the full potential of AI methods.

Clinical perspectives of the proposed machine learning model

A key limitation of existing scores is their reliance on heterogeneous cohorts treated with diverse ablation techniques and energy sources, which variably impact success rates. PFA, an emerging non-thermal ablation method, offers distinct advantages over traditional approaches. By delivering high-voltage electric fields to selectively ablate cardiac atrial, PFA minimizes collateral damage to structures like the oesophagus and phrenic nerve, enabling faster, safer, and more reproducible procedures than traditional energy sources.[13,14,25,26] Its tissue selectivity and rapid lesion delivery make it a transformative advancement in electrophysiology.[27,28] The proposed ML-based model, specifically developed for PFA patients using a standardized ablation approach, achieves an AUC of 0.75 (95% CI 0.69–0.82) for predicting procedural outcome. This model might serve as a valuable tool to prioritize patients who are likely to have high procedural success or direct to a rate control strategy patients with predicted poor outcomes (e.g. longer DAT, advanced atrial remodelling, and high BMI). The pre-procedural prediction capabilities, in any case, hold the potential to enhance workflow efficiency, identifying patients who may need adjunctive ablation strategies (e.g. posterior wall, non-PV triggers) or, after the procedure, contribute to the decision on antiarrhythmic therapy continuation or withdrawal and/or on wearable or remote monitoring follow-up plans. A key strength of this model is its reliance on simple, readily accessible, pre-procedural variables routinely collected in clinical practice, enhancing its practical applicability. Although parameters such as LA volume and BMI[29] have already shown predictive capabilities in conventional multivariate analysis, a relevant aspect of the present model lies in the comprehensive explainability, achieved through SHAP analysis and PDP/ICE plots. SHAP provides both global insights into the overall importance of features in the model and patient-specific analysis via waterfall plots, which reveal the influence of individual variables on a single patient's outcome. Notably, the global SHAP analysis confirms the importance of well-established clinical variables related to AF recurrence after catheter ablation also using different technologies, reinforcing the plausibility and reliability of the ML model. Additionally, PDP and ICE plots improve explainability by illustrating how variations in input variables can impact the predicted outcome. This complete explainability framework simplifies clinical applicability, by identifying modifiable factors that impact procedural success. For instance, as illustrated in the PDP/ICE plots in Supplementary material online, *Figure S1*, a patient's risk of AF recurrence may vary by approximately 10% if their BMI falls below 22 or rises above 26 kg/m2. Unlike traditional ablation methods, where thermal injury and variable lesion durability complicate outcome attribution, PFA's consistency, rapid learning curve (not significantly affecting procedural outcome), and tissue selectivity provide a controlled environment within which structured risk factor modification for high-risk patients awaiting treatment may impact on procedural outcome. The model is not designed to define a fixed probability cut-off for withholding ablation, in real-world practice, even a high predicted risk of recurrence may not preclude ablation in highly symptomatic patients. Optimal probability thresholds are context-dependent and would need to be defined and validated prospectively, considering patient preferences, symptom burden, and centre-specific practices. The novelty stands in the possibility to propose to a patient initially flagged at higher risk of recurrence a set of targeted interventions, moving from static risk prediction to interactive outcome optimization. The primary intended use of the model is to support shared decision-making and individualized counselling by providing risk estimates across a continuum, rather than to enforce binary treatment decisions.

Limitations

This study has several limitations that warrant consideration.

First, the sample size is relatively modest for ML applications and an external validation has not been performed, which may constrain the generalizability of the findings. At this stage, only internal validation was feasible due to the lack of access to an independent dataset. A larger and more varied dataset could enhance the model's robustness together with external (temporal and/or multicentre) validation before clinical implementation.

Second, the study exclusively focuses on patients undergoing penta-splines 12F over-the-wire PFA catheter (FARAWAVE^{TM}, Boston Scientific), limiting the model's applicability to other PFA approaches and a more direct comparison with established AF ablation risk scores that would have strengthened the added value of the proposed ML approach.

Third, some limitations of the adopted ML pipeline should be acknowledged: in particular, it cannot be excluded that kNN imputation may have introduced some noise, potentially affecting the Boruta feature selection and consequently model's discriminative performance. Moreover, missing data imputation and feature selection were not embedded within the cross-validation folds. Although this approach ensured a stable feature set across models, it does not fully meet the criteria of a strictly nested validation framework, potentially leading to slightly optimistic performance estimates. However, the adopted pipeline reflects a pragmatic trade-off commonly used in clinical ML studies and should therefore be interpreted as internally validated and exploratory. No specific strategies were implemented to explicitly address the moderate class imbalance (event rate ≈19%), and model training relied on default hyperparameter settings. Although this level of imbalance was considered unlikely to substantially affect performance, future studies should evaluate the impact of imbalance-aware training approaches and more extensive hyperparameter tuning. In addition, no formal resampling-based analysis of feature importance stability was performed.

Fourth, the model does not incorporate additional variables or clinical scenarios (as extreme LA remodelling) that could influence arrhythmia recurrence (and type, e.g. AT or flutter) risk, such as advanced pre-procedural imaging features, intra-procedural data or different energy types, delivery methods, or technological factors, potentially limiting model's predictive accuracy. However, this aligns with the deliberate design to prioritize simple, pre-procedural variables that are readily available in routine clinical practice. By simply focusing on easily accessible pre-procedural data, the model facilitates practical implementation and supports early risk stratification, enabling clinicians to optimize modifiable risk factors, such as BMI, prior to the procedure.

Finally, follow-up in ATHENA was performed according to standard clinical practice at each participating centre, was not risk-adapted, and did not involve continuous or implantable monitoring, possibly underestimating true recurrence rates. Avoiding residual heterogeneity in monitoring practices (e.g. Holter duration or number of visits across centres), AF burden data, different blanking periods, and longer follow-up (>1 year follow-up for the entire cohort) would have been required to further exclude potential source of bias; however, there was no systematic difference between patient risk groups.

Conclusion

The proposed ML–based score demonstrated good discrimination for predicting 1 year procedural outcome in patients undergoing PFA. This approach may support more individualized risk stratification and inform shared decision-making regarding rhythm-control strategies, with the potential to reduce low-yield procedures and associated risks and costs. By identifying clinical factors associated with procedural outcome, the model offers insight into determinants of success, although its role in guiding targeted interventions for modifiable risk factors requires prospective evaluation. Overall, this work represents a step towards more data-informed and patient-centred decision support in contemporary AF ablation care.

Perspectives

Competency of medical knowledge

This study enhances clinicians' ability to identify AF patients most likely to benefit from PFA. By integrating ML–based prediction into clinical decision-making, physicians can improve patient selection, optimize procedural outcomes, and allocate resources more efficiently. Understanding key predictors, such as DAT, BMI, and indexed LA volume, may support more individualized management strategies and promote data-driven, evidence-based care across all stages of professional practice.

Translational outlook

Future studies should prospectively validate this predictive model across larger and more heterogeneous populations and evaluate its integration into clinical workflows. Embedding ML algorithms into electronic health records or ablation planning systems could facilitate real-time decision support. Further research incorporating imaging, electrophysiologic, and biomarker data may enhance model precision and advance personalized approaches to AF ablation.

Supplementary material

Supplementary material is available at *Europace* online.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Conflict of interest: M.A. is consultant for Johnson & Johnson and Boston Scientific; M.M. is an employee of Boston Scientific. The other authors have no conflicts of interest to declare that are relevant to the content of this article.

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