POLISH HEART JOURNAL
Kardiologia Polska
The Official Peer-reviewed Journal of the Polish Cardiac Society since 1957
Online first
This is a provisional PDF only. Copyedited and fully formatted version will be made available soon
ISSN 0022–9032
e-ISSN 1897–4279

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Article type: Short communication

Received: August 22, 2024

Accepted: December 31, 2024

Early publication date: January 13, 2025

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Short title: AI analysis of ECG to predict AF recurrence

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INTRODUCTION

Cryoballoon-based pulmonary vein isolation (CRYO) is an effective option for rhythm control in atrial fibrillation (AF). There have been multiple attempts to predict arrhythmia recurrence. In previous study we have shown the prognostic value of increased left ventricular wall thickness (LVWT) as a novel risk factor of arrhythmia recurrence with its highest occurrence (61.9%) among patients (33.6%) with concomitant left atrial enlargement (LAE) [1]. The aim of our study is a proof-of-concept analysis if artificial intelligence (AI) analysis of electrocardiogram (ECG) signals can predict arrhythmia recurrence after CRYO, either alone or by adding prognostic value to established risk factors.

METHODS

In the current report we studied the prognostic performance of AI analysis of ECG digital signals recorded prior to CRYO for predicting arrhythmia recurrence at 2-year follow-up. Additionally, AI ECG analysis was used to search for algorithms identifying: LAE, increased LVWT. Diagnosis of LAE was upon gold-standards of LA volume by means of multislice computed tomography or echocardiography.

This is a single-center retrospective study involving 250 consecutive patients with AF, of whom 60% had paroxysmal AF. The patients underwent CRYO for de novo (72.8%) or redo ablation (27.2%). Data were obtained from the registry of patients undergoing cryoablation in the electrophysiology laboratory between May 2017 and April 2019. All patients were eligible for the procedure according to the current European Society of Cardiology guidelines, which encompass both indications and contraindications [2]. Index echocardiographic left atrial volume (LA volume) >48 cm^3/m^2 or multislice computed tomography LA volume ≥63 cm^3/m^2 identified LAE [3, 4]. Increased LVWT was defined as an echocardiographic septal/posterior wall thickness greater than 10 mm in males and 9 mm in females [3]. All patients undergoing CRYO were followed up with regular clinical visits, resting and Holter ECGs, data from implantable cardiac devices, and any available telemetry recordings, allowing precise identification of AF recurrence, defined as episodes lasting at least 30 seconds at 2 years post-procedure. The model was trained on 12-lead ECG signals sampled at 500 Hz. Initially in XML format, the signals were decoded using a Java-based decoder and saved for preprocessing. This included scaling, resampling, and filtering with a Butterworth filter. The final dataset contained signals, each with 12 leads. Due to the limited samples, transfer learning was employed to improve model performance by adapting a pre-trained model [5] through further training on our patient dataset. The fine-tuned model, based on a convolutional neural network, effectively processed the multidimensional ECG inputs, automatically extracting features without manual intervention. The pre-trained network included four dense layers, with dropout layers for stability. This approach enabled the model to retain general knowledge while integrating new data, achieving high accuracy in detecting various cardiac conditions.

Statistical analysis

Patient data were used in the statistical analysis, leading to the creation of 3 models:

- Model A: included only baseline clinical parameters: age, sex, body mass index, valvular heart disease, cardiomyopathy, hypertension, diabetes mellitus, and paroxysmal AF;

- Model B: consisted of anatomo-functional parameters: LA volume, increased LVWT, and left ventricular ejection fraction;
- Model C: contained only the results of baseline ECG AI analysis.

All models were designed to predict the recurrence of arrhythmia at 2 year post-CRYO, the analyzed data are presented in Supplementary material, *Table S1*. The one-sample Kolmogorov–Smirnov test was used to verify the distribution of continuous parameters (variables with non-normal distributions are presented as medians with an interquartile range).

The models' predictive performance was analyzed and compared using receiver operating characteristic analysis. The respective metrics computed included: area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy. All statistical analyses were performed using BM Corp. Released 2023. IBM SPSS Statistics for Windows, Version 29.0.2.0 Armonk, NY, US: IBM Corp.

RESULTS AND DISCUSSION

Arrhythmia recurrence at 2 years was 46.0% (n = 115). Median age was 61 (49.0–67.3) years. Females represented 30% of the study group. Median CHA_2DS_2-VASc score was 2.0 (1.0–3.0) and EHRA score was II (II–III) [2, 6]. Left ventricular ejection fraction <60% was observed in 29.6% of patients. The predictive performance of the studied parameters was comparable, with AUC values of 0.684 (P <0.001), 0.680 (P <0.001), and 0.669 (P <0.001) for baseline clinical (model A), anatomo-functional (model B), and AI ECG analysis (model C), respectively (Figure 1). The addition of AI findings significantly enhanced the predictive accuracy of models based on baseline clinical data alone (A + C vs. A; AUC = 0.712; P <0.001) and in combined analyses of baseline clinical and anatomo-functional data (A + B + C vs. A+B; AUC = 0.757; P <0.02).

Our model's AUC outperformed both the modified HATCH score (previously the top model for predicting arrhythmia recurrence, AUC = 0.62) and the Korean AI model, which uses demographic data and 3D reconstructed LA images from CT (0.757 vs. 0.61, respectively) [7, 8]. Predictive performance of our model appears similar to another Polish AI model (0.757 vs. 0.75, respectively), which was developed using a set of 12 most relevant variables identified from a pool of 82 variables, including also some post-procedural factors, such as early recurrence of AF, along with blood tests conducted 24 hours after the procedure [9]. The inclusion of post-procedure factors in this model limited its application for qualifying patients for the procedure. In contrast, our model, by utilizing only pre-procedure factors, can be effectively employed for this purpose.

Compared to the recent Chinese pre-ablation AI model trained on ECG, our model demonstrated inferior performance (0.757 vs. 0.84, respectively) [10]. It is important to highlight the differences between studies: a longer follow-up period averaging 2 years as opposed to 14.6 months, a broader patient population covering persistent (22%) and long-persistent AF (17.6%) not represented in the Chinese study, discrepancy in recurrence rates (46% vs. 13.5%, respectively), and sample size (250 vs. 1618).

Importantly, positive predictive value of our model was only slightly higher than that of the anatomo-functional parameter (74.2% vs. 73.1%), and its negative predictive value was lower compared to the baseline clinical parameter (70.1% vs. 72.3%). In medical practice, PPV and NPV greater than 70% indicate that our model is relatively effective at correctly identifying true positive cases as well as correctly excluding healthy individuals in contrast to the commonly used HATCH score (PPV = 66% and NPV= 59%).

Interestingly, our AI baseline ECG analysis was able to identify patients with LAE and increased LVWT, achieving AUC of 0.87. We hypothesized that our model's ability to predict AF recurrence would be based on its analysis of ECG signs of LAE and increased LVWT, regardless of the underlying rhythm on the ECG. The ongoing heat map analysis will further provide insight into this hypothesis.

While the study highlights our model's predictive capabilities, it is crucial to discuss its practical applications in clinical settings. The AI model could be integrated into clinical practice to benefit patient management in several ways: Clinicians could use the AI model to assess the risk of arrhythmia recurrence in patients undergoing ablation, guiding the decision on whether to proceed with ablation or consider alternative therapies. The AI model's predictions could inform patients about their individual risk of arrhythmia recurrence, enabling more personalized discussions about treatment options and expected outcomes. By identifying high-risk patients, the AI model could assist in tailoring post-procedural care plans, such as more intensive monitoring and adjunctive therapies to prevent recurrence.

In conclusion, prediction of recurrence after CRYO using raw ECG data with deep AI analysis is feasible. Including AI analysis of baseline ECG into the established clinical models appears to offer substantially better predictive performance. In the future, we aim to further improve our model by including larger training and test cohorts. Moreover, validation using external data will be necessary to ensure our model's efficacy and generalizability across different patient populations and clinical settings.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/polish_heart_journal.

Article information

Conflict of interest: None declared.

Funding: The study was supported by the research grant from the National Institute of Cardiology in Warsaw, Poland (2.1/V/21).

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Studied parameters	Model A	Model B	Model C	A + B	A + C	A + B + C
AUC	0.684	0.680	0.669	0.726	0.712	0.757
Sensitivity	75.0	43.7	63.4	67.9	61.6	58.9
Specificity	56.5	87.0	67.9	68.7	74.1	83.2
PPV	59.2	73.1	62.8	64.4	66.4	74.2
NPV	72.3	64.2	68.5	71.2	69.1	70.1
Diagnostic acc.	64.6	66.7	65.8	67.9	67.9	71.6
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

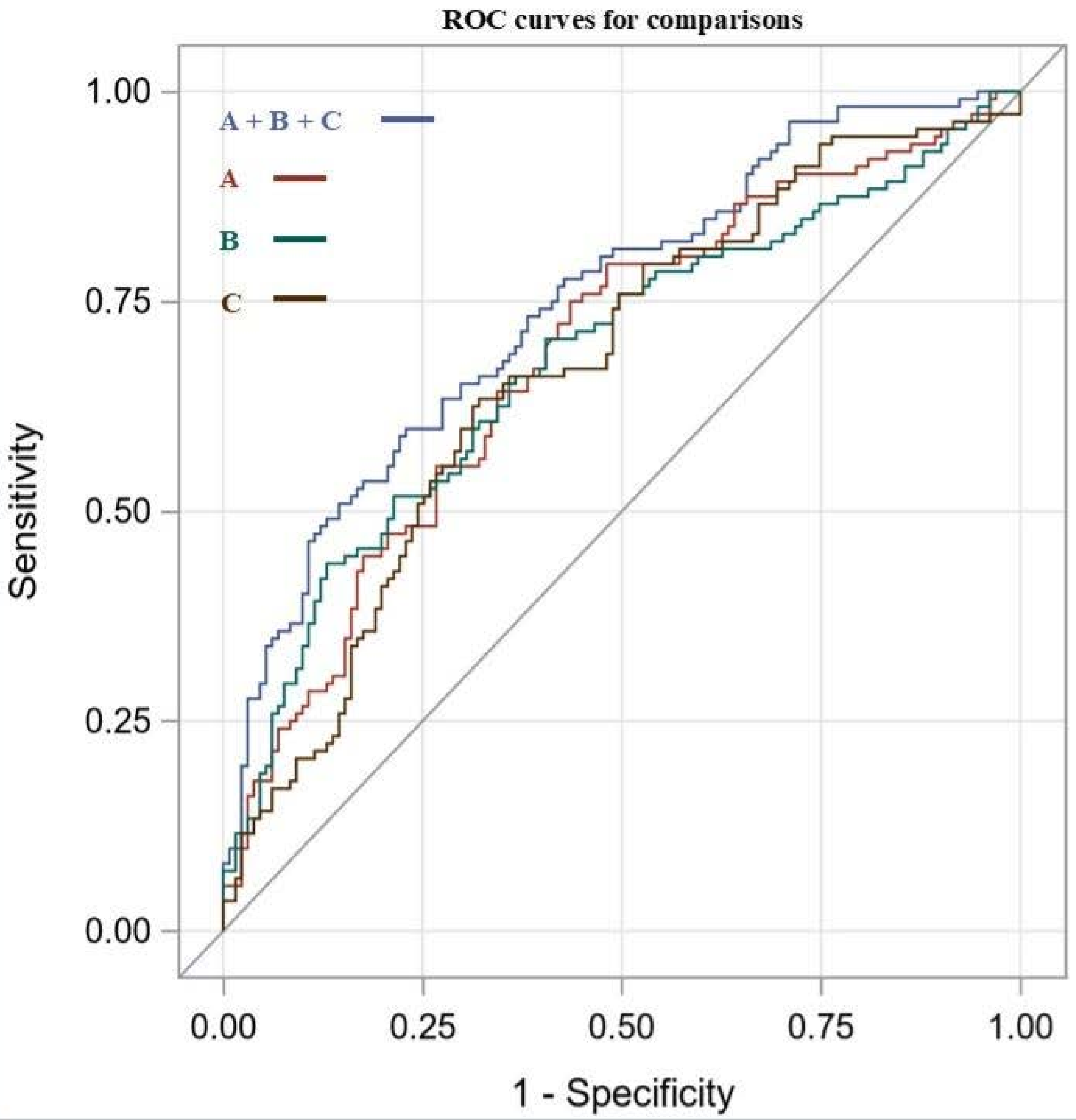

Figure 1. Predictive performance of the studied parameters

For all these parameters, the *P*-value is less than 0.001, indicating a high level of statistical significance

Abbreviations: A, baseline clinical parameter; B, anatomo-functional parameter; C, AI ECG analysis; acc., accuracy; AI, artificial intelligence; AUC, area under the curve; ECG, electrocardiogram; ↑LVWT, increased left ventricular wall thickness; LA vol, left atrial volume; LVEF, left ventricular ejection fraction; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristics