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ORIGINAL ARTICLE

Long-Term Follow-Up Results of Atrial Fibrillation Patients Who Underwent Pulmonary Vein Isolation Using the Cryoballoon and Radiofrequency Ablation and ORACL Score: A Simple Scoring System for Late Atrial Tachyarrhythmia Recurrence Prediction

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Abstract

Background: Atrial fibrillation (AF) is a common supraventricular arrhythmia affecting both elderly and younger patients. Invasive treatments, particularly radiofrequency and cryo-energy therapies, have offered varying durations of AF-free life to patients. However, despite successful invasive therapy, recurrence rates remain significant. Numerous studies have aimed to develop predictive scoring systems for AF recurrence (such as APPLE, MB-LATER, and BASE-AF). Our primary objective was, like previous AF recurrence predictors, to develop a practical yet accurate scoring system (ORACL Score) that does not rely on biochemical parameters. We compared this novel scoring system to existing recurrence prediction models.

Methods: We retrospectively reviewed 159 patients with a mean age of 55.6±10.1 who underwent second-generation CB or RF ablation between June 2014 and December 2022. All patients diagnosed with AF were questioned regarding comorbidities, and blood tests, echocardiography (TTE), complementary echocardiography (TEE), and pulmonary CT angiography were conducted. Post-procedural follow-ups were conducted at the hospital, initially at one month, then every three months, and subsequently for longer periods. Independent late atrial tachyarrhythmia recurrence predictors were defined after multivariate logistic regression analysis. Based on these estimators, the ORACL-Score system was designed. The acronym stands for "O"verweight (BMI > 28 kg/m²), "R"ecurrence occurring early, "A"F duration, "C"ategory of AF (Persistent or Paroxysmal AF), and "L" LAVI ≥ 34 ml/m².

Results: The mean follow-up period of the population was 41.9±27.4 months. Of the population, 36.5% (n=58) experienced late recurrence (LR), resulting in a tachyarrhythmia-free survival rate of 63.5%. Among these patients, 35.2% had an ORACL-Score of >2.2. Patients with LR exhibited a higher mean ORACL-Score (3.3±1.76 vs. 1.32±1.2, p<0.001) compared to those without tachyarrhythmia recurrence. ROC analysis revealed that an ORACL-Score of >2.2 successfully predicted late atrial tachyarrhythmia recurrence with a sensitivity of 70% and a specificity of 84% (AUC = 0.835, p<0.001) and was defined as an independent predictor of LR (HR: 10.1, p<0.001). Multiple prediction score systems were calculated for each patient, and a collective ROC analysis was performed for comparison purposes. The ORACL-Score maintained its superiority over former score systems with better AUC values and sensitivity/specificity values ([APPLE; AUC = 0.663, p=0.001], [MBLATER; AUC = 0.744, p<0.001], [BASE-AF$_2$; AUC = 0.754, p<0.001]).

Conclusion: The ORACL score has demonstrated effective and consistent performance as a novel recurrent prediction method in non-comorbid patients diagnosed with AF, without the requirement for additional biochemical parameters, in comparison to previous methods. It could serve as an auxiliary tool in guiding interventional clinical strategies.

Keywords: atrial fibrillation; catheter ablation; prediction; recurrence; score

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Introduction

Atrial fibrillation (AF) is a well-known supraventricular arrhythmia affecting predominantly elderly individuals, though younger patients can also be affected. The condition not only diminishes quality of life but also poses various detrimental clinical consequences.[1,2] In recent years, the treatment landscape for AF has rapidly expanded, particularly with the advent of invasive therapies such as radiofrequency and cryo-energy treatments, offering variable durations of AF-free life to patients.[3]

Despite advancements in invasive therapy, recurrence rates remain a challenge.[4,5] Predicting recurrence is vital in medical decision-making. Various biomarkers have been explored for their association with late recurrence, including left atrium (LA) diameter > 40 mm, larger left atrial volume index, and history of early tachyarrhythmia recurrence.[4,6,7] Additionally, elevated red blood cell distribution indicating pro-inflammatory activity, neutrophil/lymphocyte ratio, monocyte/high-density lipoprotein ratio, and uric acid levels have been linked to AF recurrence.[8-11]

Several scoring systems have been developed based on these parameters to predict recurrence accurately. Examples include APPLE (Age > 65 years, Persistent AF, eGFR < 60, LA diameter > 43mm, EF < 50%), MB-LATER (male, bundle branch block, LA ≥ 47mm, type of AF, and early recurrence history), and BASE-AF2 (body mass index ≥ 28 kg/m², LA dilatation ≥ 40 mm, current smoking, early recurrence, duration of AF history, Persistent AF).[12-14] The C2HEST score, tailored for patients with multiple comorbidities, is another effective predictor of late tachyarrhythmia recurrence.[15]

In our study, we retrospectively reviewed 159 patients who underwent second-generation cryoballoon (CB) or radiofrequency (RF) ablation between June 2014 and December 2022, evaluating patient characteristics, procedures, and follow-up outcomes. Our aim was to develop a practical and accurate scoring system (ORACL-Score: "O"verweight [BMI > 28 kg/m²], early "R"ecurrence, "A"F duration, "C"ategory of AF [Persistent or Paroxysmal AF], and "L" LAVI ≥ 34ml/m²) for predicting AF recurrence without relying on biochemical parameters. We compared the performance of this new scoring system against established recurrence prediction systems (APPLE, MB-LATER, and BASE-AF).

Methods

At Osmangazi University Hospital cardiology center, we perform pulmonary vein isolation (PVI) with CB and RV ablation for drug-resistant paroxysmal and persistent AF, as recommended by the guidelines.[2] A retrospective analysis of a prospectively maintained, single-center database was conducted. Exclusion criteria included being younger than 18 years, post-operative induced AF, structural heart disease, extensive dilated LA (LA diameter over 50 mm), new-onset AF developed in acute coronary syndrome process, severely progressed pulmonary comorbidity, and history of prosthetic heart valve operation. Patients who met the required criteria and had episodes of AF were considered eligible for invasive therapy. Episodes of AF lasting less than 7 days (spontaneous or treated) were defined as paroxysmal (PAF), and those lasting longer than 7 days were classified as PersAF.[2] All patients diagnosed with AF were questioned for comorbidities, and blood tests, trans-thoracic echocardiography (TTE), complementary transesophageal echocardiography (TEE), and pulmonary CT angiography were performed before proceeding to catheter ablation. In cases of late recurrence occurring after the blanking period, treatment decisions were made based on individualized rhythm or rate control plans. These patients constituted the target patient population for the risk scoring system aimed at predicting in advance. The trans-thoracic echocardiographic evaluation of each patient utilized the modified Simpson method to calculate the left ventricular ejection fraction (LVEF), with measurements taken for the left ventricular end-diastolic diameter, left atrium anterior-posterior diameter, left atrium volume index, left ventricular mass index (LV Mass), and tricuspid annular plane systolic excursion (TAPSE). Optimal criteria and normal cut-off values for these measurements were determined based on the joint guidelines of the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[16] This ensured all cardiac and pulmonary vein anatomic anomalies were visualized beforehand. Procedural (intraoperative) characteristics such as the number of freezes, freezing times, radiofrequency duration times, or warm-up times were recorded.

Catheter ablation characteristics

All antiarrhythmic drugs were discontinued at least 5 half-lives before the procedure. Transesophageal echocardiography was performed to evaluate the interatrial septum and exclude the presence of a thrombus in the left atrium within 24 hours before the procedure. All patients underwent multi-detector computed tomographic angiography to evaluate LA

and PV anatomy. Either CB or RF ablation was used for catheter ablation.[17-19] If the patient's rhythm was AF, sinus rhythm was usually achieved with electrical cardioversion before the procedure. All CB and RF PVI procedures were performed by the same electrophysiologist certified by the European Heart Rhythm Association (EHRA) with a high level of experience. A 6 French (F) decapolar catheter (St. Jude Medical) was placed in the coronary sinus, and a 6F pigtail catheter (Alvision™) was placed in the aortic root. Under fluoroscopy guidance, one transseptal (TS) puncture was performed for CB, and two TS punctures were performed for RF ablation to gain access to the LA. One TS needle (BRK-1TM, St. Jude Medical) and an 8.5F TS sheath (SL0 or SL1, St. Jude Medical) were used for TS puncture. Unfractionated heparin at a dose of 100 units per kilogram was administered after entry into the LA, followed by additional heparin boluses throughout the procedure to maintain the activated clotting time between 300 and 350 seconds.

Cryoballoon ablation was performed under conscious sedation with midazolam and fentanyl. For optimal PVI, the TS sheath was replaced with a 14F steerable sheath (FlexCath Advance™, Medtronic Inc.) over the wire. A 28-mm second-generation CB catheter (Arctic Front Advance™, Medtronic, Minneapolis, MN, USA) was used for PVI. A spiral mapping catheter (Achieve Advance™ mapping catheter 20 mm, Medtronic) delivered through the balloon was used to visualize the PV potentials. Cryoballoon was performed for 180-240 seconds in each PV antrum region after demonstrating complete occlusion of the PV ostia with 50% diluted contrast medium. If the PV potentials did not disappear within 60 seconds or early reconnection was observed, a bonus freeze was applied for the relevant PV. During isolation of the right-sided PVs, a decapolar catheter (St. Jude Medical) was introduced into the superior vena cava, and diaphragm contraction was monitored by manual palpation during freezing. Phrenic nerve pacing was routinely performed with diaphragm contraction palpation for safety purposes during all right pulmonary vein isolations. Cooling was aborted and the balloon re-engaged if even a slight reduction in contraction force was suspected. Contact force, minimum cooling temperature, cold application, and warming times in all cryoablation procedures were recorded as routine practice.

Radiofrequency ablation was performed under general anesthesia. After the double TS puncture, one steerable sheath (Agilis, St. Jude Medical, St. Paul, MN) and one 8.5F TS sheath (SL1, St. Jude Medical) were placed in the LA. The LA was mapped with multipolar catheters (Advisor HD Grid, Abbott, or Pentaray, Biosense Webster) using a three-dimensional mapping system (EnSite Precision, Abbott, or CARTO, Biosense Webster). Irrigated type sensor-enabled ablation catheters (TactiCath, Abbott, or SmartTouch Catheter, Biosense Webster) were used for PVI. Antral PVI was performed in all patients, with additional linear lesions created in a few patients according to operator preference.[18] Acute procedural success was defined as the disappearance or dissociation of all visible PV potentials. PVI was confirmed with entry and exit block maneuvers by pacing the catheters in the coronary sinus and PV.[17,18] Procedure-related features were recorded in all patients. Rapid TTE was performed pre-procedure, intra-procedure (immediately after the transseptal passage), and post-procedure to check for any complications.

Follow-up

Post-procedural follow-ups were carried out at the hospital, initially at the first month, then every 3 months, and for longer periods thereafter. Transthoracic echocardiography control and electrocardiogram (ECG) monitoring were performed within the first hour of ablations at the hospital. During the 48-hour follow-ups conducted in the hospital, ECG monitoring, assessment of newly developing complaints, and evaluation for the development of complications were conducted. Both an after-procedure (in the operating room) TTE evaluation and a bedside TTE evaluation were conducted. Anticoagulation therapy, preferably with novel oral anticoagulants, was resumed in the absence of pericardial effusion. In cases where complications developed, appropriate treatments, possibly multidisciplinary, were provided. Patients who did not develop any complications were discharged the following day.

Clinical follow-ups were scheduled at specified intervals, and patient arrhythmia history, physical examination, surface ECG, and 24-hour Holter monitoring were repeated at each visit to screen for AF recurrence. The first 3 months after the ablation

procedure were termed the "blanking period." Atrial tachyarrhythmia recurrences during the blanking period were defined as "early recurrences," while those occurring later were termed "late recurrences" (LR).[3] In patients experiencing early recurrence during the blanking period, appropriate rhythm control treatments tailored to the individual patient with recurrence were provided, which could include invasive or non-invasive approaches. All antiarrhythmic drugs were discontinued after the blanking period. In cases of late recurrence occurring after the blanking period, treatment decisions were made based on individualized rhythm or rate control plans. These patients constituted the target patient population for which the risk scoring system aimed to predict outcomes in advance.

Statistical analysis

All data were stored in electronic medical records and retrieved from there. Appropriate statistical calculation programs were used. The necessary minimum sample size for identifying meaningful independent risk factors and adequately evaluating the risk of LR was determined through appropriate power statistical analysis. Continuous variables were presented as mean values ± Standard Deviation (SD), and categorical variables as numbers (percentage). The comparison of continuous data between LR and No-LR groups was made with the unpaired t-test, while categorical data were compared using the Chi-Square test or Fischer's exact tests as appropriate. The Kolmogorov-Smirnov test was utilized to assess the normal distribution of all continuous variables. P values <0.05 were considered statistically significant.

Univariate and multivariate logistic regression analyses were performed on variables significantly related to late recurrence predictors. All variables from cryo-ablation (contact force, minimum cooling temperature, cold application, and warming times), recorded during each procedure, were grouped and analyzed alongside patient-derived variables according to the presence or absence of late recurrence. Odds ratios (OR) and confidence intervals were calculated with a P-value <0.05. These predictors were used in a post-ablation recurrence prediction score system (ORACL), and a Receiver Operating Characteristic (ROC) curve analysis was conducted. The sensitivity and specificity of the score were calculated by the area under the curve (AUC).

Score calculation and comparison

After conducting multivariate logistic regression analysis, independent predictors of LR were identified. Using these predictors, we designed the ORACL score system and compared it with prior ones. The ORACL scoring system includes the following variables: body mass index over 28 kg/m², history of early recurrence, AF duration >30 months, AF category (paroxysmal AF or persistent AF), and left atrial volume index (LAVI) ≥ 34 ml/m². Additionally, we calculated the APPLE (Age > 65 years, Persistent AF, eGFR < 60, Left Atrial Diameter > 43mm, Ejection Fraction < 50%), MB-LATER (Male, Bundle Branch Block, Left Atrium Diameter ≥ 47mm, AF Type, and Early Recurrence History), and BASE-AF2 (Body Mass Index ≥ 28 kg/m², Left Atrium Dilatation ≥ 40 mm, Current Smoking, Early Recurrence, Duration of AF History, Persistent AF) scores for each patient.

We compared the sensitivity, specificity, and AUC values of the ORACL score with those of the other predetermined prediction score systems. Furthermore, a cut-off value was determined as in previous studies.[12-14]

Results

Patient Characteristics

A total of 159 patients were evaluated for this study, with a mean age of 55.6±10.1 years. Among them, 52.8% were male. The study population comprised 79.9% PAF (n=127) and 20.1% persistent AF (PersAF) (n=32). All patients underwent their first AF ablation procedure during this study, with no prior history of AF ablation. The mean follow-up period for the overall population was 41.9±27.4 months, with no significant difference observed between the PAF and PersAF groups.

During the follow-up period, 36.5% of the study population experienced LR, resulting in a tachyarrhythmia-free survival rate of 63.5%. In the PAF group, 89.1% of patients remained tachyarrhythmia-free, whereas only 10.9% did so in the PersAF group. The mean BMI was 29.1±4.7, with 49.5% of the entire population having a BMI above 28 kg/m². A BMI >28 kg/m² was significantly more frequent in the LR group (p= 0.019). The median AF duration was 22.6±11.3 months, with 25.2% of patients having an AF history exceeding 30 months. Patients in the LR group had a significantly longer mean AF history (26±12.1 months, p= 0.019).

Table 1. Baseline characteristics of the study population.

Characteristics	All patients (n =159)	LR (n=58)	No LR (n=101)	*p* value
Gender (male), n (%)	84 (52.8)	31 (53.4)	44 (43.6)	0.229
Age, years	55.6 (±10.1)	58 (±10.4)	58 (±10)	0.485
Age >65, n (%)	16 (10.1)	7 (12.1)	9 (8.9)	0.524
Follow-up duration (months)	41.9 (±27.4)	49.5 (±25.7)	37 (±28.7)	0.246
Body mass index, (kg/m^2)	29.1 (±4.7)	29 (±5)	27.7 (±4.5)	0.129
BMI >28 kg/m², n (%)	82 (49.5)	37 (63.8)	45 (44.6)	0.019
Paroxysmal AF, n (%)	127 (79.9)	37 (63.8)	90 (89.1)	<0.001
Persistent AF, n (%)	32 (20.1)	21 (36.2)	11 (10.9)	<0.001
AF duration (months)	22.6 (±11.3)	26 (±12.1)	20 (±10.1)	<0.001
AF >30 months, n (%)	40 (25.2)	24 (41.4)	16 (15.8)	<0.001
Acute success, n (%)	157 (98.7)	56 (96.6)	101 (100)	0.255
Early recurrence, n (%)	30 (18.9)	24 (41.4)	6 (5.9)	<0.001
Systolic heart failure, n (%)	9 (5.7)	5 (8.6)	4 (4)	0.386
Hypertension, n (%)	78 (49.1)	32 (55.2)	46 (45.5)	0.242
Diabetes mellitus, n (%)	37 (23.3)	12 (20.7)	25 (24.8)	0.559
CAD, n (%)	16 (10)	6 (10.3)	10 (9.9)	1.000
TIA/Stroke, n (%)	13 (8.2)	5 (8.6)	8 (7.9)	1.000
OSAS, n (%)	10 (6.3)	4 (6.9)	6 (5.9)	1.000
Alcohol consumption, n (%)	4 (2.5)	2 (3.4)	2 (2.0)	0.966
Current smoking, n (%)	21 (13.2)	6 (10.3)	15 (14.9)	0.419
$CHADS_2VASc$ score	1.67 (±1.2)	1.83 (±1.2)	1.57 (±1.2)	0.235
LVEF (%)	59.8 (±9)	62 (±10.3)	62 (±8.1)	0.156
LV end-diastolic diameter, mm	48.4 (±4.3)	50 (±4.8)	47.6 (±3.7)	0.001
LA diameter, mm	39 (±4.3)	41 (±4.0)	37.8 (±4.1)	<0.001
LAVI ≥34 ml/m², n (%)	70 (44)	37 (63.8)	33 (32.7)	<0.001
LAVI, mm	33.3 (±12.8)	37.9 (±12.4)	30.7 (±12.3)	0.001
LV Mass Index, g/m²	97.25 (±22.7)	93.40 (±20.4)	103.95 (±25.19)	0.005
TAPSE, mm	24.1 (±3.9)	23.2 (±3.6)	24.6 (±4)	0.030
Haemoglobin g/dl	13.9 (±1.7)	13.65 (±1.8)	14.4 (±1.6)	0.202
eGFR, ml/min/1.73m²	87 (±19.9)	86.9 (±20.4)	89.9 (±19)	0.635
Oral anticoagulant, n (%)	118 (74.2)	49 (84.5)	69 (68.3)	0.025
RAS blocker, n (%)	64 (40.2)	27 (46.6)	37 (36.6)	0.785
Beta-blocker, n (%)	106 (66.7)	40 (69)	66 (65.3)	0.641
Amiodarone, n (%)	43 (27)	20 (19.8)	23 (39.7)	0.009
Propafenone, n (%)	46 (28.9)	33 (32.7)	13 (22.4)	0.170
ORACL	2.07 (±1.74)	3.3 (±1.76)	1.32 (±1.2)	<0.001
APPLE	0.59 (±0.82)	0.95 (±0.98)	0.39 (±0.53)	<0.001
MB-LATER	0.89 (±0.77)	1.36 (±0.81)	0.62 (±0.61)	<0.001
BASE-AF2	1.35 (±1.25)	2.02 (±1.1)	0.96 (±0.92)	<0.001

AF = Atrial Fibrillation; BMI = Body Mass Index, CAD = Coronary Artery Disease, eGFR = estimated Glomerular Filtration Rate, LA = Left Atrium, LR = Late recurrence of Atrial Fibrillation, LV = Left Ventricle, LVEF = Left Ventricular Ejection Fraction, LVH = Left Ventricular Hypertrophy, MRA = Mineralocorticoid Receptor Antagonist, OAD = Oral Anti-Diabetic, OSAS = Obstructive Sleep Apnea Syndrome, TAPSE = Tricuspid Annular Plane Systolic Excursion, TIA= Transient Ischemic Attack, RAS= Renin–Angiotensin system

Early recurrences occurred in 11.7% of the study population, with a significantly higher incidence in the LR group (41.4%, p<0.001). Among patients with early recurrence, recovery occurred spontaneously in 16.7%, while 40% were treated with pharmacological cardioversion, 63.7% with electrical cardioversion, and 2% with radiofrequency ablations. Patients who reverted to sinus rhythm spontaneously or underwent pharmacological or electrical cardioversion had a significantly higher recurrence rate of tachyarrhythmia compared to those who did not receive further intervention (p= 0.40, p<0.001, and p= 0.002, respectively).

The mean hemoglobin level was 14.7±1.6 mg/dl, and the mean estimated glomerular filtration rate (eGFR) was 89±19.5 ml/min/1.73m², with no significant difference observed between the LR and No-LR groups. The mean left ventricular EF was 59.8 ±9%, the mean LA diameter was 39±4.3 mm, and the mean LAVI was 33.3±12.8 ml/m² in the entire population. Dilated LA (>40 mm) and LV diastolic diameters were significantly higher in the LR group (p<0.001 for both). A LAVI cut-off value of 33.5 ml/m² (62% sensitivity and 70% specificity) was defined using ROC hazard analysis. Patients with LAVI ≥ 34 ml/m² were significantly more prevalent in the LR population (p<0.001). Comparisons of clinical, laboratory, and echocardiographic parameters between these two groups are presented in Table 1.

Table 2. Procedural characteristics of the study population.

Characteristics	All patients (n =159)	LR (n=58)	No LR (n=101)	*p* value
Complete successful PVI, n (%)	154 (96.9)	54 (93.1)	100 (99.0)	0.040
RSPV successful PVI, n (%)	157 (98.7)	57 (98.3)	101 (100)	0.186
RIPV successful PVI, n (%)	156 (98.1)	56 (96.6)	100 (99.0)	0.273
LSPV successful PVI, n (%)	157 (98.7)	56 (96.6)	101 (100)	0.060
LIPV successful PVI, n (%)	158 (100)	58 (100)	101 (100)	-
Total procedure duration, min	85 (±55.5)	87.5 (±61.8)	80 (±51.3)	0.184
Total fluoroscopy time, min	21 (±6.5)	22 (±5.9)	20 (±5.9)	0.173
Total complications, n (%)	23 (14.4)	10 (17.2)	13 (12.8)	0.451
Cardiac tamponade, n (%)	4 (2.5)	2 (3.4)	2 (2)	0.569
Pericardial effusion, n (%)	7 (4.4)	2 (3.4)	5 (5)	0.657
Phrenic nerve palsy, n (%)	1 (0.6)	0 (0)	1 (1)	1.000
Groin complications, n (%)	4 (2.5)	4 (2.5)	0 (0)	0.007
TIA, n (%)	1 (0.6)	0 (0)	1 (1)	1.000
Major bleeding, n (%)	4 (2.5)	2 (3.4)	2 (2)	0.581

LIPV = Left Inferior Pulmonary Vein, LSPV = Left Superior Pulmonary Vein, RIPV = Right Inferior Pulmonary Vein, RSPV = Right Superior Pulmonary Vein, PVI = Pulmonary Vein Isolation, TIA= Transient Ischemic Attack

Procedural characteristics

A total of 630 (99.0%) out of 636 PVs were acutely isolated during the procedure, and complete and successful PVI was significantly less common in the LR group (p= 0.040). Procedural characteristics and complications are provided in Table 2. Pericardial effusions occurred in 4.4% of cases (n=7), while cardiac tamponades occurred in 2.5% of patients (n=4) and were successfully drained. Groin complications were experienced by 2.5% of patients (n=4), and major bleeding occurred in 2.5% of cases (n=4). Temporary phrenic nerve palsy (PNP) and transient ischemic attack (TIA) occurred once in one patient each. Among all these complications, groin complications were significantly more common in the LR group (Table 2).

None of the other procedural variables, including contact force, minimum cooling temperature, cold application, and warming times, showed any significant relationship with late recurrence.

Recurrence prediction and ORACL score

Univariate analysis was performed on variables that showed a significant correlation with LR. Body mass index over 28 kg/m², AF history longer than 30 months, history of early recurrence during the blanking period, presence of PersAF before the procedure, and having a LAVI ≥34 ml/m² were determined as significant predictors of late post-ablation AF recurrence with a p-value <0.05. Consequently, these predictors were entered into a multivariate logistic regression analysis to identify independent predictors. In this analysis, except for the history of PersAF, the other variables retained their significance and were defined as independent predictors of LR.

However, the history of PersAF was retained as a fifth score parameter based on its high significance in the univariate analysis and its demonstrated recurrence effects in previous studies (Table 3). The ORACL name was derived from the initials of these variables (Overweight, early Recurrence, AF duration, Category of AF, and LAVI ≥34 ml/m²). β values, acquired during the analysis, were set as coefficients to determine the weight of each variable, and they were summed up for the final ORACL score calculation (Figure 1). The ROC curve was plotted to estimate the predictive power of the ORACL score (Table 4). Additionally, APPLE (Age >65 years, PersAF, eGFR <60, LA Diameter >43mm, EF <%50), MB-LATER (male, bundle branch block, LA ≥ 47mm, type of AF, and early recurrence history), and BASE-AF2 (BMI ≥ 28 kg/m², LA dilatation ≥ 40 mm, current smoking, early recurrence, duration of AF history, PersAF) scores were calculated for comparison.

Table 3. Multivariate logistic regression results.

Parameter	β value	Odds Ratio	95% CI for EXP Lower	Upper	p value
BMI >28 kg/m²	1.125	3.081	1.308	7.259	0.004
AF duration >30 months	1.350	3.858	1.587	9.382	<0.001
Persistent AF history	0.765	2.149	0.795	5.810	0.132
Early recurrence	2.643	14.060	4.623	42.762	0.012
LAVI ≥34 ml/m²	1.044	1.282	6.296	2.841	0.039

AF = Atrial Fibrillation, BMI = Body Mass Index, LAVI = Left Atrial Volume Index

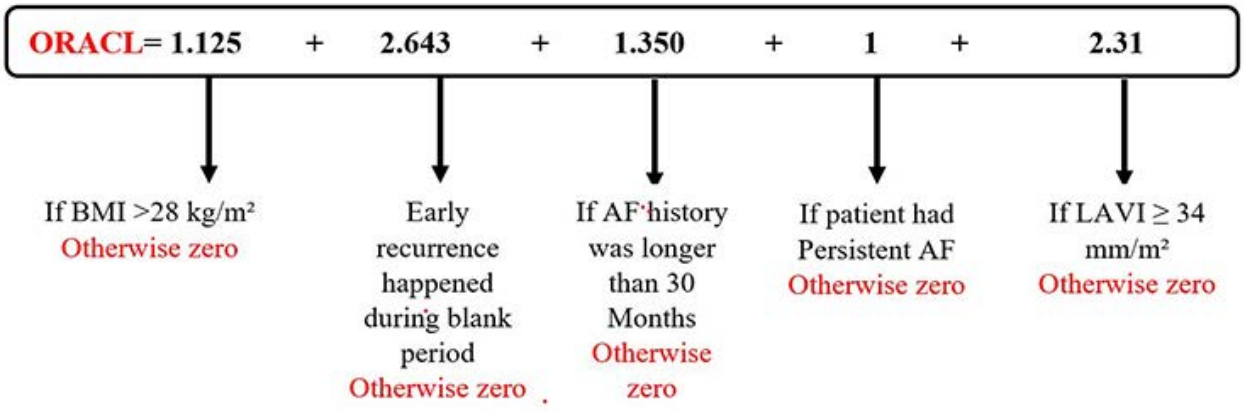

Figure 1. ORACL score calculation.

Score comparison

The ORACL score exhibited the highest prediction capability with an AUC of 0.835, 95% Confidence Interval (CI) (0.76 to 0.9), and a p-value < 0.001. The BASE-AF2 score system also demonstrated high predictive performance in this population, although the AUC level was lower at 0.754, 95% CI (1.75 to 4.94) (p < 0.001). The MB-LATER scores were the second most effective system in our population, but the AUC level was also lower at 0.744, 95% CI (0.665 to 0.823) (p < 0.001). The APPLE score was the third statistically significant scoring system, with a moderate quality AUC of 0.663, 95% CI (0.572 to 0.831) (p = 0.001).

The ROC comparison of risk scores for the overall population is presented in the ROC curve in Figure 2, and Kaplan-Meier survival analysis of the overall population is shown in Figure 3.

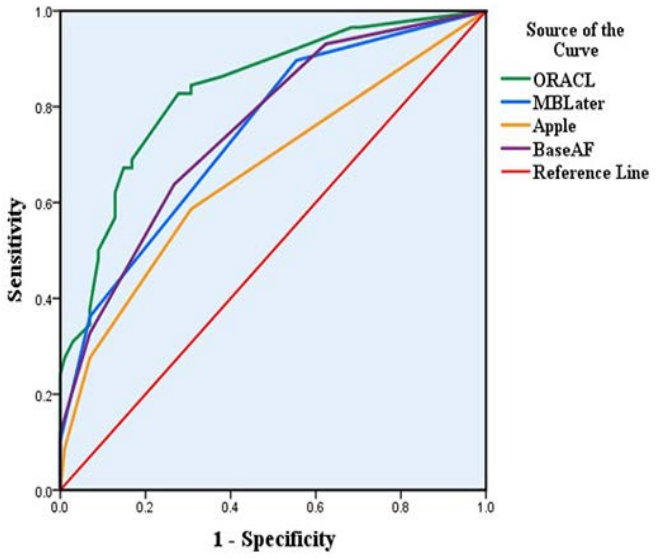

Figure 2. ROC comparison of risk scores.

Table 4. ROC comparison table

Test Result Variable(s)	Area Under the Curve	95% Confidence Interval		p value
		Lower	Upper	
ORACL	0.835	0.769	0.900	<0.001
APPLE	0.663	0.572	0.754	0.001
MB-LATER	0.744	0.665	0.823	<0.001
BASE-AF2	0.754	0.677	0.831	<0.001

Discussion

In this comprehensive study, we investigated the short and long-term performance as well as procedural characteristics of CB ablation (CBA) and RF procedures conducted at our university. We identified independent predictors of LR and incorporated them into the ORACL late recurrence prediction score. The ORACL scores were then compared against existing risk scores, and they exhibited the highest predictive capability, as indicated in previous studies.[12-14]

Follow-up and recurrence predictors

In a mixed population of patients with PAF and PersAF, we achieved an acute procedural success rate of 98.7% and a tachyarrhythmia-free survival rate of 63.5% in the entire population, with a tachyarrhythmia-free survival rate of 89.1% in the

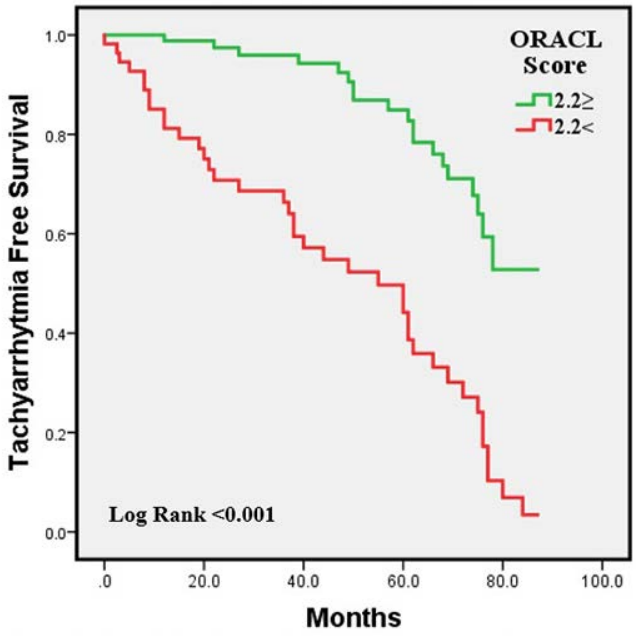

Figure 3. Kaplan-Meier analysis of overall population.

PAF patient subgroup over three and a half years of follow-up following a single ablation procedure. Previous observational studies have demonstrated the safety and efficacy of both CBA and RF-based AF ablation. These follow-up studies have shown similar percentages of long-term tachyarrhythmia-free survival over shorter durations. Aytemir et al. reported a 90% tachyarrhythmia-free rate at 10 months, Canpolat et al. achieved 81% at one year, and Hara et al. reported 70% at three years, all with PAF patients exclusively.[14,20,21] Over the past nearly 42 months, 36.5% of our study population experienced late atrial tachyarrhythmia recurrences. Takarada et al., in a comparable mixed population, also previously reported a LR rate of 29.5% over 38 months of follow-up, similar to our findings.[22] In our population, the most common cause of AF recurrence after CBA and RF ablations was PV reconnection (51.7%, n=30). All these patients underwent secondary RF catheter ablation.

Despite various ablative treatment strategies, LR remains the most common obstacle. Several observational studies in the literature have addressed this issue. Consistent with other studies, factors such as LA diameter (LAD),[1] BMI over 28,[2] history of early recurrence,[3] and persAF history[4] showed significant correlations in our population. Additionally, longer AF duration[5] also showed a significant relationship with LR, similar to findings by Canpolat et al. In contrast to Kornej et al.[12] (APPLE) where age, left ventricular EF, and renal dysfunction were significant parameters, in our study, they were not significant, possibly due to our younger population with fewer comorbidities. Similar to our findings, Mujović et al.[13] (MB-LATER) identified AF type and early recurrence history as predictors of LR. However, in their study, bundle branch block, LA diameter >47 mm, and male gender were independent predictors of recurrence, unlike in our population. The differences in findings could be attributed to variations in patient demographics and comorbidities. As recent AF guidelines suggest, comorbidities, older age, and dilated cardiac chambers correlate significantly with AF incidence and persistence.[13] Early intervention with fewer risk factors tends to yield better clinical outcomes.[2] Therefore, the ORACL score could serve as a valuable tool for risk assessment in early-stage patients before the onset of advanced age or comorbidities.

Complications

In our population, complications were limited. A total of 23 patients (14.4%) experienced procedure-related complications, among which 4 patients (2.5%) were related to groin bleeding. One patient (0.6%) was diagnosed with PNP, and another (0.6%) experienced a TIA; however, both fully recovered during the follow-up period. Additionally, seven patients (4.4%) developed pericardial effusion, and four patients (2.5%) required drainage due to cardiac tamponade. Aytemir et al. also reported 9 cases (8.26%) of PNP and 8 cases (7.3%) of pericardial effusion in their CB study.[20] In Canpolat et al.'s study population, a total of 14 patients (5.8%) experienced procedure-related complications, including two cases (0.8%) requiring drainage due to cardiac tamponade, one case of arteriovenous fistula, and three cases of transient PNP. The remaining complications were related to groin bleeding.[14] Similarly, Hara et al. reported 11 cases (5.9%) of PNP but no instances of pericardial effusion.[21] In alignment with the findings of these studies, we assigned a non-operator clinician to physically monitor diaphragmatic movements during right phrenic nerve pacing while isolating the right PVs. Ablation procedures were halted at the slightest suspicion of nerve palsy. Compound muscle action potential (CMAP) monitoring was not universally performed in all procedures and was not statistically analyzed. However, TTEs were conducted just before the procedure, after trans-septal passage, at the conclusion of the procedure, and repeated two hours later. Oral anticoagulation was resumed in all patients without pericardial effusion.

ORACL score

With this study, we developed a scoring system incorporating the previously identified independent predictors of LR. Each β value was assigned as an individual risk constant and aggregated to derive the final score for each patient. Additionally, we applied other established risk prediction score systems for comparison. An ORACL score >2.2 exhibited 70% sensitivity and 84% specificity (AUC = 0.835, 95% CI 0.769-0.900, $p<0.001$) in our study population. This indicates that patients with a score exceeding 2 are more likely to experience LR after ablative PVI therapy. High-risk patients should undergo closer monitoring and may benefit from secondary medical or ablative therapies.

Canpolat et al. also introduced a scoring system (BASE-AF2) with similar objectives. The BASE-AF2 score system had a cut-off level of 3 points and demonstrated a sensitivity of 80.8% and a specificity of 91.6% (AUC = 0.94; 95% CI: 0.89–0.97, p<0.001), displaying robust prediction performance in our population. However, the AUC level was slightly lower at 0.754 (95% CI 0.677-0.831, p< 0.001) compared to ORACL.[14] This discrepancy could be attributed to different predictor parameters, such as smoking, sleep apnea, and LA dilation over 40 mm, which were more prevalent in their population. ORACL is designed to guide initial treatment decisions in newly diagnosed patients with fewer comorbidities and normal-sized hearts. The unpredictability of early recurrence before the procedure when using ORACL, similar to BASE-AF2, may be considered a limitation. However, we propose that ORACL score results should be updated after the blanking period following catheter ablation.

Mujović et al.'s MB-LATER score is another AF post-ablation recurrence prediction score system, but unlike ORACL, it identifies bundle branch block, LA diameter > 47 mm, and male gender as independent predictors. The MB-LATER score exhibited a similar performance to BASE-AF2 with an AUC of 0.744 (95% CI: 0.66–0.82, p<0.001), which can be attributed to differing population characteristics.[13]

Kornej et al. previously introduced another prediction scoring system, APPLE, with parameters such as age, left ventricular EF, and renal dysfunction. Although these parameters differed from those in our study, we applied APPLE to our population for comparison purposes and achieved an AUC of 0.663 (95% CI: 0.572–0.754, p<0.001).[12]

The utilization of the ORACL score for patient risk assessment before and after the procedure could provide valuable insights to electrophysiologists throughout the ablation process. By evaluating the benefits and risks of invasive therapy initially for patients with high ORACL scores, operators can exercise greater caution in creating optimal PV isolation lines and planning follow-up after CBA and RF ablation. Further large-scale validation studies are necessary to confirm our findings and demonstrate the clinical utility of the ORACL score in real-world practice.

Limitations

As previously mentioned, this study was prospectively designed but conducted retrospectively at a single center. All data were collected during routine follow-up visits and documented in patients' medical records. Due to the duration of the study, not all patients were monitored for the same length of time. Intervals between visits varied, spanning months, and continuous monitoring was not feasible. As a result, recurrences during these intervals may have been missed, or patients might not have reported them during visits (referred to as silent PAF). Scheduled clinic examinations, ECGs, and short-term Holter rhythm monitoring during these visits may have underestimated episodes of AF recurrence.

The key variables in the ORACL scoring system partially overlapped with those in former recurrence prediction systems. With a larger and multi-center study, it's possible that these variables could align more closely and lead to higher prediction performance. Conducting such a study could provide more robust evidence and improve the accuracy of recurrence prediction in patients undergoing AF ablation.

Conclusion

This study on PVI demonstrates that interventional AF therapy is a reliable, successful, and relatively safe treatment option for patients with PAF. Moreover, it represents a significant treatment approach for cases of PersAF.

Factors such as being overweight, longer duration of AF exposure, higher LA volume (≥ 34 ml/m²), history of persAF, and early recurrence post-ablation are independently associated with recurrence. The ORACL score provides practitioners with a tool to make concrete and realistic predictions regarding post-ablation tachyarrhythmia-free follow-up periods. Patients without comorbidities or advanced cardiac diseases can be evaluated for recurrence risk, and treatment strategies can be tailored accordingly. This approach allows for careful assessment of the potential benefits and risks for each patient prior to intervention.

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Conflict of Interests

None

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