

Left atrial diameter, CHA₂DS₂-VASc score and type of atrial fibrillation predict pulmonary vein isolation outcome

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Abstract

Purpose Pulmonary vein isolation (PVI) is the most effective treatment strategy for atrial fibrillation (AF). This study evaluated Pulmonary Vein Isolation Outcome Degree (PVIOD) as a new semi-quantitative measure for PVI success after a 7-year follow-up and determined predictors associated with PVIOD.

Methods We enrolled 117 patients with symptomatic AF who underwent PVI and after a 7-year follow-up applied PVIOD with 4 possible outcomes. PVIOD 1 group included patients with successful single PVI. PVIOD 2 group included patients with efficacy after ≥ 2 re-PV isolation and/or additional substrate modification (ASM). PVIOD 3 group contained subjects with clinical success after PVI \pm ASM. Patients with procedural and clinical failure were in PVIOD 4 group.

Results In multivariate ordinal logistic regression analysis PVIOD was independently associated with longstanding persistent AF with paroxysmal AF as referent category: odds ratio (OR) 4.1, 95% confidence interval (95% CI) 1.3-12.8 (P=0.014), left atrial (LA) diameter: OR 1.2, 95% CI 1.1-1.3 (P<0.001) and CHA₂DS₂-VASc score: OR 1.5, 95% CI 1.0-2.2 (P=0.039). LA size, CHA₂DS₂-VASc score and AF type predicted 7-year probability for procedural and procedural with clinical failure. LA diameter >41mm (AUC 0.741, 95% CI 0.6-0.8, P<0.001) and CHA₂DS₂-VASc score ≥ 2 (AUC 0.718, 95% CI 0.6-0.8, P<0.001) predicted long-term procedural and clinical failure.

Conclusion PVIOD is a new classification for PVI success. LA diameter, CHA₂DS₂-VASc score and AF type are independently associated with PVIOD and predict procedural and procedural with clinical failure after the 7-year follow-up. LA diameter >41mm and CHA₂DS₂-VASc score ≥ 2 predict long-term PVI failure.

1 Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia associated with increased morbidity and mortality [1]. Radiofrequency (RF)-based pulmonary vein isolation (PVI) is an established therapy for symptomatic, drug-refractory paroxysmal and persistent AF [2]. The story of PVI began two decades ago with modest and promising efficacy [3]. In the modern era, after multiple catheter ablations and additional substrate modification (ASM), long-term success was 62-79.5% in paroxysmal AF, 46.2–68.2% in persistent AF and 39–41% in longstanding persistent AF [3–7]. Many studies have explored the predictors of arrhythmia recurrence, such as non-paroxysmal AF, female sex, longer AF duration prior to the catheter ablation, sleep apnea, obesity, elderly patients, hypertension, structural heart disease, enlarged left atrial (LA) diameter, higher CHADS₂, CHA₂DS₂-VASc, MB-LATER and APPLE scores, low LA voltage, C-reactive protein and increased LA fibrosis detected by cardiac magnetic resonance imaging [8–12].

Numerous trials evaluated the efficacy of PVI and usually used a qualitative measure with 2 possible outcomes, successful or ineffective procedure [2, 7]. Our study aimed to evaluate Pulmonary Vein

Isolation Outcome Degree (PVIOD) as a new semi-quantitative measure for PVI success after a 7-year follow-up and to determine parameters for predicting the PVIOD.

2 Methods

This prospective study included 124 consecutive patients with symptomatic AF who underwent PVI at the Institute for Cardiovascular Diseases Dedinje, from January 2012 to December 2013. AF was classified according to the 2012 HRS/EHRA/ECAS Consensus Statement on Catheter and Surgical Ablation of AF [10]. Paroxysmal or persistent AF was defined, respectively, if there was a success or failure to terminate AF spontaneously or with intervention within 7 days of onset. Longstanding persistent AF was diagnosed if arrhythmia lasted more than 1 year. The study excluded those who had permanent AF, pregnancy, acute reversible causes of AF, myocardial infarction that occurred within 3 months, moderate-to-severe valvular stenosis or regurgitation and coronary artery disease indicated for revascularization procedure.

The trial was approved by the Ethics Committee of the Institute for Cardiovascular Diseases Dedinje. Work was conducted in accordance with the Declaration of Helsinki. All patients signed informed consent prior to inclusion in the study. Initially, all patients were evaluated for age, gender, AF duration, AF type, clinical symptoms and signs, body mass index, CHA₂DS₂-VASc score, risk factors for cardiovascular disease (hypertension, hypercholesterolemia and diabetes mellitus), the presence of structural heart disease and usage of antiarrhythmic drugs (AAD) prior to the PVI. All medical documents, 12-lead electrocardiograms (ECG) and 24-h Holter monitorings were reviewed for the presence of AF. Transthoracic echocardiography measured the end-systolic LA size through antero-posterior diameter from parasternal long-axis view. Transesophageal echocardiography (TEE) was used to exclude the presence of thrombus in left auricula and LA. 64-multislice computed tomography of pulmonary veins (PVs) together with images from TEE provided better visualization of LA and PVs anatomy because of significant inter- and intra-patient variability in the number, size and bifurcation of the PVs.

2.1 Ablation protocol

In all patients, the first PVI included only catheter ablation of PV antrum without additional substrate modification (ASM). After trans-septal puncture, an intravenous bolus of heparin (5.000 IU) was administrated, followed by additional doses to maintain activated clotting time between 300 and 350s. During the procedure, the antrum of ipsilateral PVs was widely encircled with an irrigated tip catheter (ThermoCool Navi-Star, Biosense-Webster) with point-by-point ablation lesions using the CARTO system. The RF energy was applied at a target temperature of 43 degrees Celsius with a power limit of 30–35 W for 30–60 seconds. Entrance block, exit block and non-inducibility of AF confirmed the initial success of PVI. When typical atrial flutter (AFL) was documented, cavotricuspid isthmus was ablated.

All subjects received AAD for 3 months after initial PVI, a daily oral dose of either 200mg amiodarone or 150mg propafenone 3 times a day or 80mg sotalol twice a day. Oral anticoagulation was administrated for 6 months after catheter ablation in all patients and continued after that in those with a high CHA₂DS₂-

VASc score. Repeated procedures were performed in case of AF recurrences with re-PV ablation in patients with recovered PV conduction. In those subjects without PV reconnection, ablation of complex fractionated atrial electrograms and/or additional substrate strategies were applied based on observations made during the electrophysiology study. ASM included LA roof line, mitral annular isthmus, anterior line, inferior line, lines around superior vena cava and coronary sinus.

2.2 Follow-up

AF type and burden were determined 1, 3 and 6 months after catheter ablation, and later by at least annual clinical review. During visits, ECG and 24-h Holter monitoring were performed for rhythm evaluation. Recurrences of AF, AFL and atrial tachycardia (AT) were defined as episodes of arrhythmias lasting for more than 30s. Subjects who could not be reached were excluded from the study.

We introduced a new semi-quantitative method for measuring PVI success, i.e. Pulmonary Vein Isolation Outcome Degree (PVIOD) with 4 possible outcomes after a 7-year follow-up: PVIOD 1 group included patients with successful single PVI; PVIOD 2 group included subjects with efficacy after ≥ 2 re-PV isolation and/or ASM; Patients with clinical success after PVI \pm ASM regardless of procedure number were in PVIOD 3 group; PVIOD 4 group contained patients with procedural and clinical failure despite PVI \pm ASM. Clinical success was defined as a significant reduction ($\geq 70\%$) in the number and duration of AF episodes with or without AAD.

2.3 Statistical analysis

Continuous variables are presented as the mean \pm standard deviation or median and interquartile range, while categorical variables are showed as absolute values and percentages. The differences between continuous values were assessed using an unpaired Student's t-test when the data were normally distributed, a Mann-Whitney test for skewed variables and λ^2 test or Fisher's exact test for nominal variables. Ordinal logistic regression analysis was used to identify the predictors for PVIOD. Multivariate (MV) logistic regression analysis included variables with a statistical significance of 0.05 on the univariate (UV) logistic regression model. Nomogram as a two-dimensional diagram was used for graphical presentation of MV logistic regression model prediction. Receiver operating characteristic (ROC) curves were applied to determine the cut-off points for LA diameter and CHA₂DS₂-VASc score. Significance was established at $P < 0.05$.

3 Results

3.1 Study population

Initial PVI was performed in 124 patients but 7 subjects did not respond for evaluation and were excluded from this trial. Baseline and PVIOD characteristics of 117 study patients are shown in Table 1. The mean age of the subjects was 56.2 ± 8.5 years, 93 patients (79.5%) were male, 75 (64.1%) had hypertension, 9 (7.7%) diabetes mellitus and 53 (45.3%) had hypercholesterolemia. Structural heart disease was present in 21 subjects (17.9%): ischaemic heart disease in 7 patients (6%), dilated cardiomyopathy in 9 (7.7%),

valvular heart disease in 4 (3.4%) and hypertrophic cardiomyopathy in 1 patient (0.8%). The mean LA diameter was 41.9 ± 4.7 mm, mean CHA₂DS₂-VASc score 1.4 ± 1.1 point, 77 patients (65.8%) were in paroxysmal AF, 24 (20.5%) in a persistent form of arrhythmia and 16 (13.7%) in longstanding persistent AF. The mean duration of AF prior to the PVI was 5 (1–18) years. Three patients (2.6%) had tachy-brady sick sinus syndrome of which 2 (1.7%) had implanted DDDR pacemakers. During the initial PVI procedure, typical AFL was diagnosed in 8 subjects (6.8%) and cavotricuspid isthmus was successfully ablated in all of them.

Table 1
Baseline and PVIOD characteristics of the study patients

Parameter	All n = 117	PVIOD 1 n = 38	PVIOD 2 n = 34	PVIOD 3 n = 17	PVIOD 4 n = 28
Age (years)	56.2 ± 8.5	56.0 ± 7.8	54.3 ± 9.4	59.8 ± 8.3	56.8 ± 8.3
Gender (male)	93 (79.5%)	30 (78.9%)	30 (88.2%)	14 (82.4%)	19 (67.9%)
Duration of AF (years)	5 (1–18)	5 (1–16)	4 (1–16)	8 (1–18)	5.5 (2–15)
Paroxysmal AF	77 (65.8%)	31 (81.6%)	22 (64.7%)	12 (70.6%)	12 (42.9%)
Persistent AF	24 (20.5%)	5 (13.2%)	10 (29.4%)	2 (11.8%)	7 (25%)
Longstanding persistent AF	16 (13.7%)	2 (5.3%)	2 (5.9%)	3 (17.6%)	9 (32.1%)
BMI (kg/m ²)*	27.7 ± 4.0	26.9 ± 4.3	27.8 ± 4.1	27.5 ± 3.4	28.6 ± 3.8
CHA ₂ DS ₂ -VASc score	1.4 ± 1.1	1.2 ± 0.9	0.9 ± 1.1	1.7 ± 1.3	1.9 ± 0.9
Hypertension	75 (64.1%)	24 (63.2%)	16 (47.1%)	12 (70.6%)	23 (82.1%)
Diabetes mellitus	9 (7.7%)	2 (5.3%)	1 (2.9%)	1 (5.9%)	5 (17.9%)
Hypercholesterolemia	53 (45.3%)	18 (47.4%)	12 (35.3%)	11 (64.7%)	12 (42.9%)
Structural heart disease	21 (17.9%)	5 (13.2%)	3 (8.8%)	3 (17.6%)	10 (35.7%)
Left atrial diameter (mm)	41.9 ± 4.7	39.3 ± 3.8	41.9 ± 4.6	43.1 ± 5.1	44.7 ± 3.9
Propafenone	33 (28.2%)	15 (39.5%)	8 (23.5%)	4 (23.5%)	6 (21.4%)
Betablocker	70 (59.8%)	23 (60.5%)	19 (55.9%)	9 (52.9%)	19 (67.9%)
Antyarrhythmic group III	68 (58.1%)	17 (44.7%)	22 (64.7%)	12 (70.6%)	17 (60.7%)
Verapamil	5 (4.3%)	3 (7.9%)	0 (0.0%)	0 (0.0%)	2 (7.1%)

Results are shown as number (percentage), mean ± standard deviation or as median (interquartile range). PVIOD, Pulmonary Vein Isolation Outcome Degree; AF, atrial fibrillation; BMI, body mass index; * n = 93 patients.

In 117 study patients, we performed 209 catheter ablations (mean 1.8 per patient). Fifty-three patients had 1 PVI while 64 patients underwent redo ablations: 41 had 2 procedures, 18 had 3 ablations and 5 had 4 procedures. Arrhythmias complications were found in 8 patients (6.8 %) of whom 3 had left-sided AT and 5 had atypical AFL. During follow-up, 3 patients died from non-cardiac causes which were not related to PVI. In the total number of 209 procedures, there were 18 complications (8.6%), of which 7 (3.3%) were major and 11 (5.3%) were minor.

3.2 Catheter ablation success after seven-year follow-up

The mean duration of follow-up after the first and last ablation was, respectively, 83 ± 10 and 64 ± 22 months. PVIOD 1 group included 32.5% (n = 38) of patients with successful single PVI. PVIOD 2 group included 29.1% (n = 34) of patients who underwent ≥ 2 successful catheter ablations: re-PVI in 24.8 % (n = 29) cases and ASM in 4.3% (n = 5) cases. PVIOD 3 group contained 14.5% (n = 17) of subjects with clinical success after PVA ± ASM. PVIOD 4 group contained 23.9% (n = 28) of patients with procedural and clinical failure.

Seven-year success after single PVI was 32.5%, of which 40.2% in paroxysmal AF, 20.8% in persistent AF and 12.5% in longstanding persistent AF (Table 2). Cumulative long-term PVI success after single and multiple procedures with ASM was 61.6%: in paroxysmal AF 69.4%, persistent AF 62.5% and longstanding persistent AF 25%. Cumulative procedural and clinical success after the 7-year follow-up was 76.1%: in paroxysmal AF 85%, persistent AF 70.8% and longstanding persistent AF 43.7%.

Table 2

Success after a single PVI, multiple procedures, and clinical success in patients with paroxysmal, persistent and longstanding persistent atrial fibrillation

	Paroxysmal AF	Persistent AF	Longstanding persistent AF	All
	n = 77	n = 24	n = 16	n = 117
PVIOD 1	40.2	20.8	12.5	32.5
PVIOD 2	29.2 (69.4)	41.7 (62.5)	12.5 (25)	29.1 (61.6)
PVIOD 3	15.6 (85)	8.3 (70.8)	18.7 (43.7)	14.5 (76.1)
Results are shown as percentage (%) for success (cumulative success). AF, atrial fibrillation; PVI, pulmonary vein isolation; PVIOD 1, Pulmonary Vein Isolation Degree 1 – success after single PVI; PVIOD 2 – success after multiple procedures; PVIOD 3 – clinical success				

3.3 Predictors for unsuccessful catheter ablation of pulmonary vein

In UV ordinal logistic regression analysis PVIOD was independently associated with longstanding persistent AF with paroxysmal AF as referent category: odds ratio (OR) 6.5, 95% confidence interval (95% CI) 2.3–18.6 (P = 0.001), LA diameter: OR 1.2, 95% CI 1.1–1.3 (P < 0.001), CHA₂DS₂-VASc score: OR 1.5, 95% CI 1.1–2.1 (P = 0.008), structural heart disease: OR 3.0, 95% CI 1.2–7.2 (P = 0.014) and diabetes mellitus: OR 3.6, 95% CI 1.0–13 (P = 0.049) (Table 3). In MV ordinal logistic regression model PVIOD

remained independently associated with longstanding persistent AF with paroxysmal AF as referent category: OR 4.1, 95% CI 1.3–12.8 (P = 0.014), LA diameter: OR 1.2, 95% CI 1.1–1.3 (P < 0.001) and CHA₂DS₂-VASc score: OR 1.5, 95% CI 1.0-2.2 (P = 0.039).

Table 3
Univariate and multivariate ordinal logistic regression analysis

Predictor	OR	UV 95% CI	P-value	OR	MV 95% CI	P-value
Age (years)	1.0	1.0-1.1	0.43	Referent	0.4–2.7	0.923
Gender (male)	1.5	0.7–3.5	0.289	1.0	1.3–12.8	0.014
Duration of AF (years)	1.1	1.0-1.2	0.127	4.1	1.0-2.2	0.039
Paroxysmal AF	Referent	0.8–4.4	0.124	1.5	0.6–11.7	0.217
Persistent AF	1.9	2.3–18.6	0.001	2.6	0.4–2.8	0.962
Longstanding persistent AF	6.5	1.0-1.2	0.173	1.0	1.1–1.3	<0.001
BMI (kg/m ²)*	1.1	1.1–2.1	0.008	1.2		
CHA ₂ DS ₂ -VASc score	1.5	0.3–3.5	0.105			
Hypertension	1.8	1.0–13	0.049			
Diabetes mellitus	3.6	0.5-2.0	0.895			
Hypercholesterolemia	1.0	1.2–7.2	0.014			
Structural heart disease	3.0	1.1–1.3	<0.001			
Left atrial diameter (mm)	1.2	0.2–1.1	0.086			
Propafenone	0.5	0.6–2.2	0.695			
Betablocker	1.1	0.9–3.4	0.109			
Antyarrhythmic group III	1.7	0.1–3.1	0.545			
Verapamil	0.6					

UV, univariate ordinal logistic regression; MV, multivariate ordinal logistic regression; OR, Odds ratio; CI, confidence interval; AF, atrial fibrillation; BMI, body mass index; * n = 93 patients.

Nomogram 1 was configured for 3 risk factors: LA diameter, CHA₂DS₂-VASc score and type of AF, which affected the 7-year probability for procedural failure (PVIOD 1 + PVIOD 2 as procedural success compared with PVIOD 3 + PVIOD 4 as procedural failure) (Fig. 1). Nomogram 2 showed the influence of the same risk factors on the seven-year probability for procedural and clinical failure (PVIOD 1 + PVIOD 2 + PVIOD 3 as procedural and clinical success compared with PVIOD 4 as procedural and clinical failure) (Fig. 2).

By using ROC curve, optimal cut-off values were calculated for LA diameter 41.5mm and for CHA₂DS₂-VASc score 1.5. LA 1 ROC curve (procedural success compared with procedural failure) had a sensitivity of 67% and a specificity of 80% with AUC 0.726, 95% CI 0.6–0.8, P < 0.001 (Fig. 3). LA 2 ROC curve (procedural and clinical success compared with procedural and clinical failure) had a sensitivity of 86%, a specificity of 60% and AUC 0.741, 95% CI 0.6–0.8, P < 0.001.

CHA₂DS₂-VASc score 1 ROC curve (procedural success compared with procedural failure) had a sensitivity of 58% and a specificity of 74% with AUC 0.711, 95% CI 0.6–0.8, P < 0.001 (Fig. 4). CHA₂DS₂-VASc score 2 ROC curve (procedural and clinical success compared with procedural and clinical failure) had a sensitivity of 68%, a specificity of 71% and AUC 0.718, 95% CI 0.6–0.8, P < 0.001.

4 Discussion

To the best of our knowledge, this is the first study that presented and used semi-quantitative assessment for PVI success which we called Pulmonary Vein Isolation Outcome Degree. PVIOD 1 stands for patients with the best result of catheter ablation while PVIOP 4 refers to the worst outcome of patients. Until now the trials usually used a qualitative measure of PVI success with 2 possible outcomes: effective or unsuccessful procedure [2, 5, 7].

After a 7-year follow-up, a single PVI had a modest success of 32.5% in our study group, with the best result of 40.2% in patients with paroxysmal AF, 20.8% in persistent AF and as low as 12.5% in longstanding persistent AF. Numerous trials detected long-term success after single catheter ablation from 29–57% [2, 4, 5, 7]. Repeated ablations without ASM, after the 7-year follow-up, increased cumulative success in our study to 57.3%. Additional substrate strategies with an efficacy rate of 4.3% made very small benefit to procedural success which increased to 61.6%. In the study by Teunissen et al., the efficacy of additional substrate ablations was 4.2%, which magnified procedural success to 62.5% [2]. The work of Ouyang et al. showed that patients with paroxysmal AF and normal left ventricular ejection fraction after single PVI (4.8-year follow-up) had a success rate of 46.6%, after the second procedure 73.9% and after the third ablation the efficacy was 79.5% [4]. Our results were satisfactory in patients with paroxysmal AF; after the first PVI and the 7-year follow-up, the success rate was 40.2%, and after the last ablation success was 69.4%.

In our patients, long-term clinical success was reported in 14.5% of subjects which increased cumulative success to 76.1% with excellent result in paroxysmal AF (85%), good outcome in persistent AF (70.8%) and modest efficacy in longstanding persistent AF (43.7%). These data show the importance of clinical improvement and the role of AAD therapy in AF management. Therefore, long-term clinical success (on top of procedural success) is a very significant outcome. Teunissen et al. found that clinical improvement on or off AAD was 25% and increased cumulative success to 87.5% in the total population of 509 study patients [2].

The most challenging issue in managing patients with AF is identifying those predictors for unsuccessful ablation. A large number of studies determined the risk factors for poor outcome following PVI as non-paroxysmal AF (particularly longstanding persistent AF), LA dilatation and higher CHA₂DS₂-VASc score, which was confirmed in our trial [2, 8, 9, 12]. In our study, MV ordinal logistic regression analysis found an independent association between PVIOD and LA diameter, CHA₂DS₂-VASc score and AF type. LA diameter > 41mm was a high predictor of procedural failure (AUC 0.726) and procedural with clinical failure (AUC 0.741) in our patients. LA enlargement is a well-known risk factor for AF, associated with atrial electroanatomical remodeling, which plays the main role in the perpetuation and progression of AF [11]. The computational model confirmed that a critical LA effective conducting size > 40mm was required for sustained multiple wavelet reentry [11]. A meta-analysis of D'Ascenzo et al. showed that persistent AF, LA diameter > 50mm and arrhythmia recurrences within the first month after catheter ablation are the most powerful predictors of procedural failure [12]. PVI success is highly dependent on atrial disease stage and enlarged LA is widely accepted as a predictor of AF recidivism.

Our study determined that CHA₂DS₂-VASc score ≥ 2 was a predictor of poor PVI outcome. Patients with CHA₂DS₂-VASc scores 0 and 1 displayed successful ablations, but those with other scores showed high predictive value for procedural failure (AUC 0.711) and procedural with clinical failure (AUC 0.718). A score of ≥ 2 for both CHADS₂ and CHA₂DS₂-VASc scores had the highest predictive value for AF recurrence after single catheter ablation for paroxysmal AF in the study of Letsas et al. [13]. In a relatively small cohort of patients with longstanding persistent AF, it was shown that CHA₂DS₂-VASc score ≥ 3 and renal dysfunction were significantly associated with ablation failure within 31 months [14]. Other scores, like APPLE, DR-FLASH and MB-LATER predicted electro-anatomical substrate and arrhythmia recurrences in patients with AF who underwent catheter ablation [15]. The identification of specific markers before PVI in patients with AF defines the best candidates for the procedure and future ablation responders. Prediction of arrhythmia recurrences is complex because of the influence of disease stage, patients' comorbidities, operators' experience, equipment for ablation, etc.

In the current study, UV ordinal logistic regression analysis showed an association of PVIOD with structural heart disease and diabetes mellitus, but not in the MV model. Structural heart disease is a well-known predictor of early and very late recurrence of AF after RF ablation [9]. Cardiac risk factors such as hypertension and diabetes mellitus are closely correlated with inflammation and consequently with atrial fibrosis and remodeling [16]. Although in our MV analysis it does not reach significance, the importance of diabetes mellitus prevention and treatment in AF patients is obvious.

In our study nomograms presented a seven-year probability for procedural failure and for procedural with clinical failure, which were predicted with 3 risk factors: LA diameter, CHA₂DS₂-VASc score and type of AF. Determination of AF type, CHA₂DS₂-VASc score and measurement of LA diameter could provide an easy and available way of predicting catheter ablation outcome.

PVIOD is a new PV ablation outcome scoring system. This classification considers the number and efficacy of PVI, clinical success, optional additional substrate modification and antiarrhythmic therapy.

The scoring of PVIOD is a novel way of assessing PVI success since other studies with standard instruments rate PVI efficacy by procedural success or failure. The novelty of our results is an independent association between PVIOD and 3 clinical parameters: LA diameter, CHA₂DS₂-VASc score and type of AF, after a 7-year follow-up. These risk factors are very convenient to predict future PVI outcomes and easy to be measured already at baseline with cardiac echocardiography and clinical evaluation of patients. By using nomograms we can calculate both long-term procedural failure and procedural with clinical failure for patients with AF who will be treated with PVI.

This study showed significant major ablation complications in 3.3% of procedures, which is acceptable and can compare with the result (2.5-8%) from other eminent electrophysiology laboratories [17, 18]. There were no deaths connected to catheter ablations in our patients which are the excellent results.

5 Study Limitations

This study is limited because of the relatively small sample size and being a single-centre trial. PVIOD as a new semi-quantitative measure for PVI success needs to be tested in future studies with a more homogenous and larger group of patients, especially to confirm the influence of diabetes mellitus and structural heart diseases in the genesis of atrial fibrillation.

6 Conclusion

This study developed Pulmonary Vein Isolation Outcome Degree as a new semi-quantitative measure for PVI success. LA diameter, CHA₂DS₂-VASc score and AF type were independently associated with PVIOD and predicted PVI outcome after the 7-year follow-up. LA size > 41mm and CHA₂DS₂-VASc score ≥ 2 predict long-term procedural and procedural with clinical failure.

Abbreviations

AAD	Antiarrhythmic drugs
AF	Atrial fibrillation
AFL	Atrial flutter
ASM	Additional substrate modification
AT	Atrial tachycardia
ECG	Electrocardiogram
LA	Left atrial
MV	Multivariate

PV	Pulmonary vein
PVI	Pulmonary vein isolation
PVIOD	Pulmonary Vein Isolation Outcome Degree
RF	Radiofrequency
TEE	Transesophageal echocardiography
UV	Univariate

Declarations

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest that is relevant to the content of this article.

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Code availability SPSS statistics 22.0 software (IBM, USA) was used for statistical analysis.

Consent to participate All authors had access to the data used in this study and participated in writing the manuscript. The authors confirm that this manuscript is original and that no portion is under consideration elsewhere in another journal. None of the paper's contents have been previously published. All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Consent for publication This publication has been read and approved by all authors, as well as by the responsible authorities at the Institute for Cardiovascular Diseases Dedinje, where the work has been carried out. The deidentified participant data will be shared on a request basis. Please directly contact the corresponding author to request data sharing. We will share statistical analysis plan, the data base with all patients' data: clinical, echocardiography, radiofrequency ablations characteristics etc. The data will be available immediately after the publication and will be shared on a request basis for anyone. Any type of analysis will be available and we will send the data through e-mail with fine explanations.

Authors' Contributions

Conceptualization: Ruzica Jurcevic is guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Ruzica Jurcevic coordinated study, analyzed the data, wrote the manuscript as first author and is the corresponding author; **Methodology:** Ruzica Jurcevic, Lazar Angelkov; **Formal analysis and investigation:** Ruzica Jurcevic, Velibor Ristic, Dejan Vukajlovic; **Writing-original draft preparation:** Ruzica Jurcevic;

Writing-review and editing: Lazar Angelkov, Petar Otasevic, Nebojsa Tasic; **Supervision:** Lazar Angelkov, Milovan Bojic

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Figures

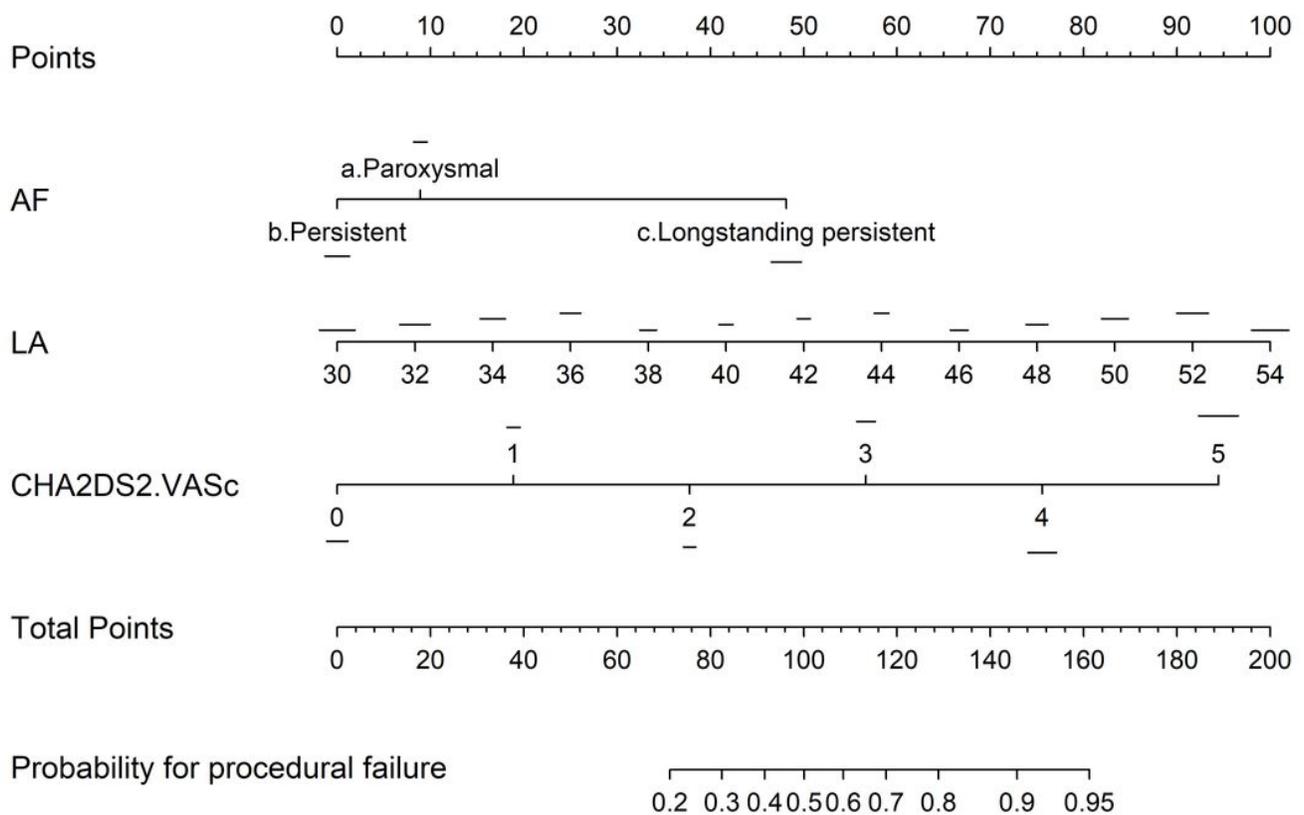


Figure 1

Nomogram 1 shows the influence of AF type, LA diameter and CHA2DS2-VASc score on the 7-year probability for procedural failure. Instruction for using the nomogram: perpendicularly draw a line from the axis of each risk factor to the top line labeled "Points" and summarize the number of points. Then draw a line from the axis called "Total Points" to the axis which measure probability for procedural failure after the 7-year follow-up. AF, atrial fibrillation type: a. Paroxysmal, b. Persistent, c. Longstanding persistent; LA, left atrial diameter, CHA2DS2-VASc, CHA2DS2-VASc score

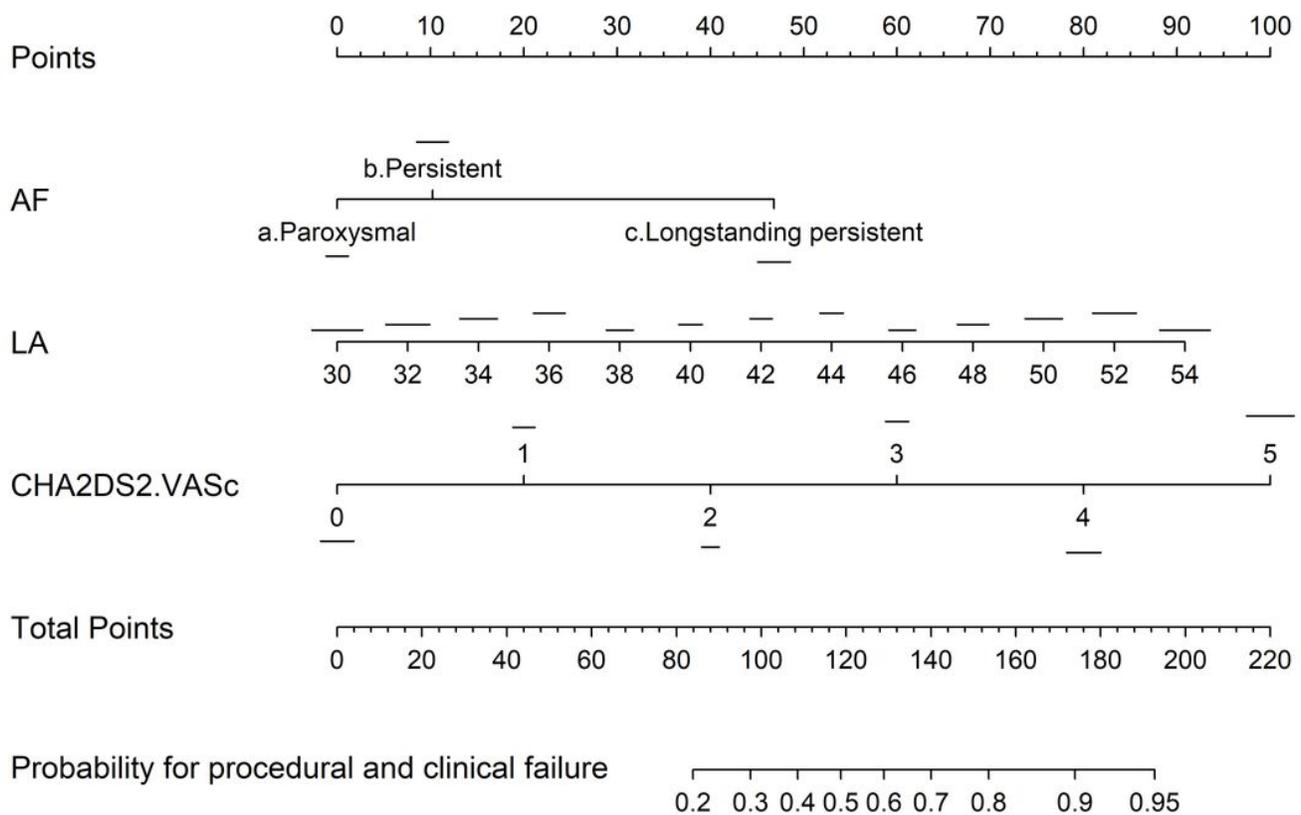


Figure 2

Nomogram 2 shows the influence of AF type, LA diameter and CHA2DS2-VASc score on the 7-year probability for procedural and clinical failure. AF, atrial fibrillation type: a. Paroxysmal, b. Persistent, c. Longstanding persistent; LA, left atrial diameter, CHA2DS2-VASc, CHA2DS2-VASc score

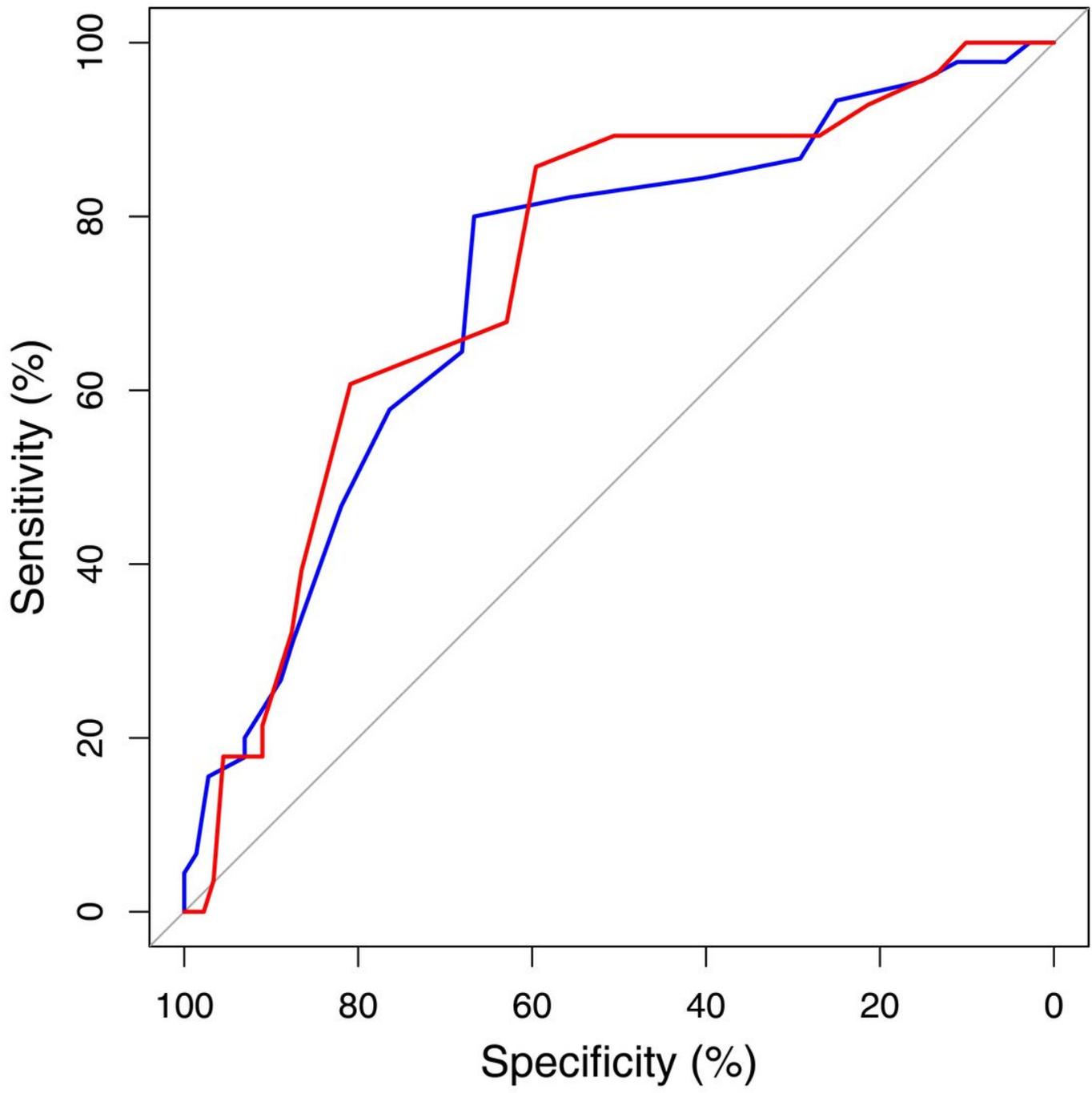


Figure 3

Receiver operating characteristic (ROC) curves for left atrial diameter. blue curve: procedural success compared with procedural failure; red curve: procedural and clinical success compared with procedural and clinical failure

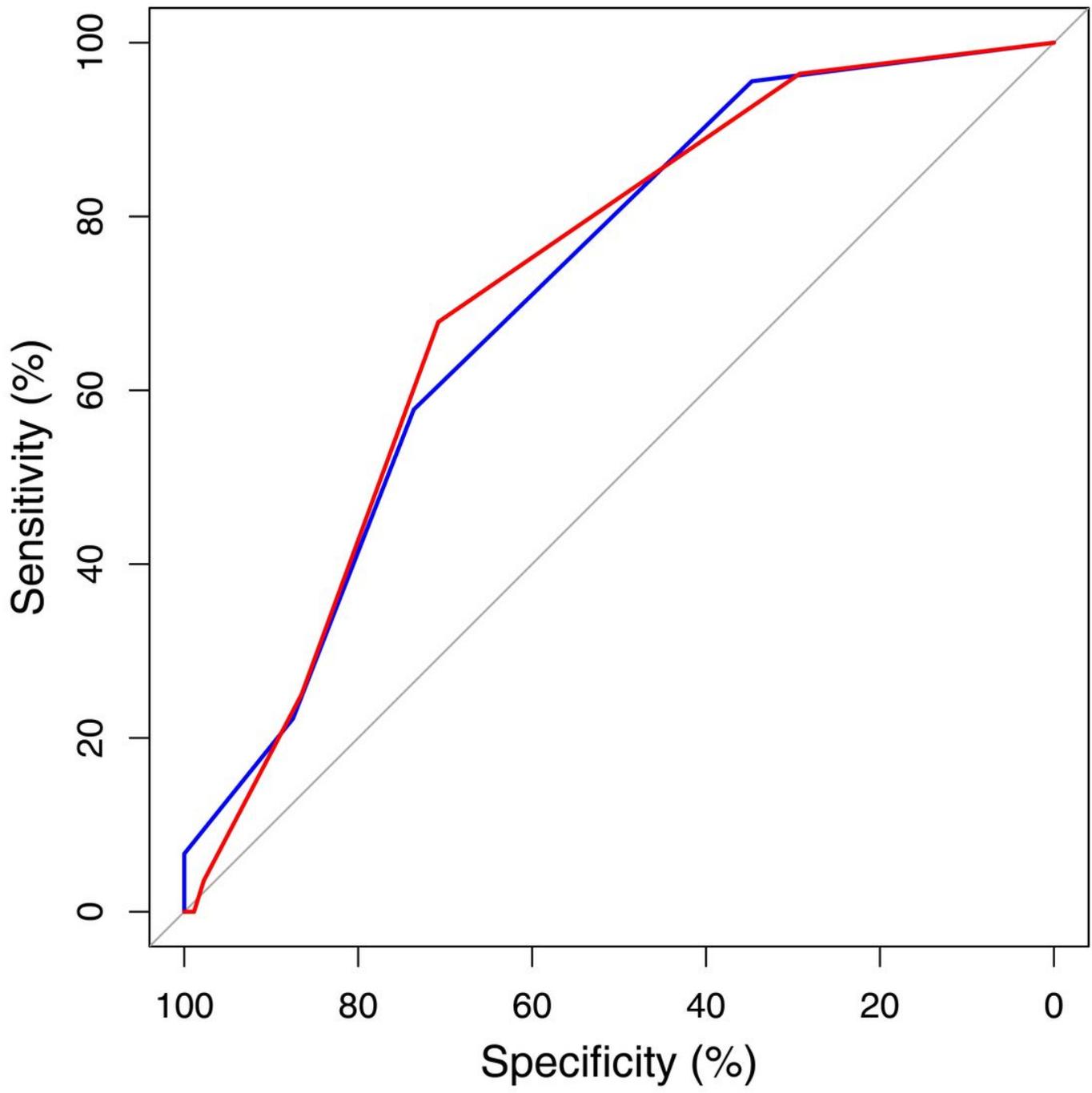


Figure 4

Receiver operating characteristic (ROC) curves for CHA2DS2-VASc score. blue curve: procedural success compared with procedural failure; red curve: procedural and clinical success compared with procedural and clinical failure