Novel Predictors For New Onset Atrial Fibrillation After Typical Atrial Flutter Ablation: An Invasive Prospective Study

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Abstract

Purpose: Patients undergoing cavotricuspid isthmus (CTI) ablation for typical flutter (AFL) have a high incidence of new onset atrial fibrillation (AF). We aimed to analyze the incidence and predictors for new onset AF in this subset of patients to stratify thromboembolic risk.

Methods: Between 2016 and 2019, 70 patients without history of AF but with high-risk for developing AF, based on a recent AFL ablation or a high PACE score for AF risk, were prospectively included. All patients were monitored continuously by implantable loop recorder and followed by remote monitoring.

Results: Overall 48 patients were included after CTI ablation and 22 patients were included based on a high PACE score. New onset AF rate at 12 months was significantly higher in the AFL group compared to PACE group (56.3% vs 22.7%, p=0.011). History of AFL was the only independent predictor for new onset AF (HR:3.82; 95% CI:1.46-10.03; p=0.006) at a median follow-up of 12 months (Q1-Q3:4-19 months). In the AFL group, two very strong independent predictors for new onset AF were a PACE score ³30 (HR:6.9; 95% CI:1.71-27.91; p=0.007) and HV interval ³55 (HR:11.86; 95% CI:2.57-54.8; p=0.002).

Conclusions: AFL is the most important predictor for new onset AF. In patients undergoing AFL ablation, a high PACE score and/or long HV interval predict even higher risk, and may be useful in decision for empiric long-term anticoagulation.

Introduction

Typical atrial flutter (AFL) is caused by a macroreentry in the right atrium and can be easily eliminated by cavotricuspid isthmus (CTI) catheter ablation, with a recurrence-rate of 6%, decreasing to 1.5% if very specific techniques are used to assess complete CTI block [1–3]. However, after AFL ablation, new onset atrial fibrillation (AF) is diagnosed in 20 to 50% of cases at 2–3 years [4–13]. AF detection increases with more frequent monitoring and/or longer follow-up duration [8,9]. Several studies have identified predictors for AF after AFL ablation, but all are retrospective and non-invasive. On note guidelines aim for documentation of AF in the decision making process of continuation/discontinuation of long-term anticoagulation.

To date, the strongest predictors for AF after AFL ablation are left atrium dilatation [6,7], its surface ECG surrogate, the presence of advanced interatrial block [10], and its electrophysiological surrogate, the presence of a long interatrial conduction time [11]. Other variables associated with new onset AF are a high HATCH score [12], AF inducibility during the CTI ablation procedure [13], and the presence of obstructive sleep apnea (OSA) [9,14].

In this study we sought to analyze the incidence and predictors for new onset AF after CTI ablation for typical AFL in a prospective manner, and compare with patients without AFL, but with high risk for AF based on the PACE calculator score. All patients underwent internal loop recorder (ILR) implantation or

had preexisting implantable cardiac device with an atrial lead (CDAL) for continuous long-term monitoring.

Methods

Study setting

This study was supported by the 2014 La Marató de TV3 Foundation Program, which was dedicated to heart diseases and aims to promote biomedical research through the funds raised by Catalonian donations. The study was reviewed and approved by the Hospital del Mar ethics committee and all ablation procedures and ILR implantations were performed after written informed consent was obtained.

Patient population

Between 2016 and 2019, patients with high risk to develop AF and no history of AF were considered to be included in this prospective single-centre study. Patients were considered high risk if they had at least one of the two following conditions:

1. Patients presenting with typical AFL, undergoing CTI ablation with resultant complete bidirectional block.

2. Patients with a PACE calculator risk score ≥ 30% for new onset AF at 3 years. The PACE calculator score uses a composite of 4 independent predictors for new onset AF (age, heart failure/cardiomyopathy, supraventricular ectopy > 0.2% or atrial tachycardia on 24h-holter monitoring (SVE), and PR interval) to predict new onset AF at 3 years [15]. This calculator is available at https://afibcalculator.com. An example can be seen in Fig. 1.

All patients underwent a 24h-holter monitoring to evaluate atrial ectopy, and an ILR implantation except for those already wearing a CDAL, and were followed by remote monitoring. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by our institution's human research committee.

Study endpoints

The introductory endpoint was the incidence of new onset AF after CTI ablation compared to other high risk patients with no history of AFL. Any AF episode of at least 2 minutes was defined as positive. The precise primary endpoint was the study of multiple clinical, echo, ECG, and electrophysiological variables to predict new onset AF after CTI ablation.

Electrophysiological study, CTI ablation and ILR implantation.

The description of the procedure has been described previously [16]. Briefly cavotricuspid isthmus ablation was performed under local anesthesia and conscious sedation. Anticoagulation therapy was not discontinued. Two diagnostic multipolar steerable 6F catheters were placed through the right femoral

vein into the low lateral right atrium and the coronary sinus ostium (CSO). A 7F irrigated-tip catheter was used for CTI mapping and ablation. Radiofrequency ablation was performed during atrial pacing from the CSO or during AFL. Established criteria for the diagnosis of bidirectional CTI complete block were assessed, including incremental pacing maneuvers [16–18]. Conduction parameters, including AH and HV interval were measured. During the same procedure, an ILR was placed under local anesthesia and antibiotic prophylaxis with Cefazolin.

Long-term follow-up

All antiarrhythmic drugs were discontinued after ILR implantation. Patients had follow-up in the outpatient clinics 2 months after the procedure and every 6 months thereafter for a minimum period of time of 1 year. Patients were monitored with monthly remote transmissions by means of Home Monitoring Service Center (Biotronik ILR) or Merlin.net (Abbott ILR).

Statistical analysis

Continuous variables are expressed as mean ± SD. Comparisons between groups were performed using an unpaired Student t test, a Chi-square test or a Fisher exact test analysis as appropriate. The primary end point was AF documentation, first of all taking into account the whole population and afterwards, restricted to the population having with previous AFL. Kaplan–Meier survival curves were performed to compare patients with and without previous AFL, using log-rank test to check differences between survival curves. Cox regression models were used to estimate hazard ratios associated to AF. Univariate and multivariate analysis were performed. Variable selection on multivariate analysis was based on previous knowledge (clinical criteria) and variables with p-values < 0.1 on univariate analysis (both criteria combined). Finally, and restricted to the analysis of patients with previous AFL, optimal cutoffs points were calculated for the variables PACE calculator score and HV, using the Youden criteria: sample point that maximizes the Youden index (sensitivity + specificity − 1). These dichotomized variables were also analyzed through Kaplan-Meier survival curves and included in the multivariate analysis. A p value of $\leq$ 0.05 was considered statistically significant. All statistical analyses were performed using STATA version 15.1 (StataCorp, College Station, TX, USA).

Results

Population characteristics

Between 2016 and 2019, 70 patients (79% male, 78.54 ± 10.87 years) with high risk to develop AF and no history of AF were included: 48 patients (85% male, 76.11 ± 10.68 years) were consecutive non-selected patients included after CTI ablation with complete bidirectional block (AFL group) independent of the PACE calculator risk score, and 22 patients (64% male, 80.59 ± 10.74 years) were included based on a high PACE calculator score (PACE group). Overall 60 patients (86%) underwent an ILR implantation during admission, while the remaining 10 patients (14%) had a previously implanted CDAL. There were either no complications related to the ablation procedure or to the ILR implantation. Patients with previous AFL had

less comorbidities, including renal failure, hypertension, dyslipidemia, left ventricle hypertrophy, previous stroke, ischemic coronary disease and valvular disease (Table 1). As expected, the PACE calculator score was lower among patients with previous AFL (20.09 ± 19.3 with AFL vs. 47.05 ± 20.77 without AFL; $p < 0.001$), as the history of AFL was the only reason for them to be enrolled, whereas patients without AFL were selected for their higher PACE calculator score. For the same reason CHA2DS2-VASC score was higher in patients without AFL compared to those with AFL (4.5 ± 1.4 vs 2.7 ± 1.6, respectively; $p < 0.001$). No differences were observed in terms of ECG, echocardiography, Holter or polysomnography parameters between both groups.

Table 1
Comparison of characteristics in patients who had prior AFL ablation and patients who did not, but had high-risk score for AF

	Total population (n = 70)	Without AFL (n = 22)	With AFL (n = 48)	p-value
Clinical variables				
Age (years) mean (SD)	78.54 (10.87)	80.59 (10.74)	76.11 (10.87)	0.079
BMI (kg/m2) mean (SD)	30.10 (5.51)	29.92 (4.17)	30.18 (5.99)	0.885
Glom. F (ml/min) mean (SD)	65.10 (19.40)	55.82 (16.89)	69.54 (19.10)	0.019
Hemoglobin (mg/dL) mean (SD)	13.70 (1.95)	13.07 (2.11)	13.99 (1.82)	0.115
Hypertension	55 (78.5%)	21 (95.4%)	34 (70.8%)	0.026
Tobacco use	31 (44.3%)	7 (31.8%)	24 (50%)	0.303
Diabetes mellitus	23 (32.8%)	7 (31.8%)	16 (33.3%)	1.000
Dyslipidemia	39 (55.7%)	17 (77.3%)	22 (45.8%)	0.020
Ischemic disease	21 (30%)	11 (50%)	10 (20.8%)	0.023
Valvular disease	9 (12.8%)	7 (31.8%)	2 (4.2%)	0.003
Stroke	7 (10%)	6 (27.3%)	1 (2.1%)	0.003
CHA2DS2-VASC	3.2 (1.8)	4.5 (1.4)	2.7 (1.6)	< 0.001
PACE-Calc. mean (SD)	28.41 (23.28)	47.05 (20.77)	20.09 (19.30)	< 0.001
Polysomnography variables				
Snorer	29 (41.4%)	8 (27.6%)	21 (72.4%)	0.610
Epworth. mean (SD)	8.68 (4.28)	8.09 (3.99)	8.92 (4.45)	0.642
IAH. mean (SD)	31.95 (19.48)	26.00 (16.63)	34.60 (20.34)	0.157
CT90%. mean (SD)	17.90 (27.93)	12.54 (24.55)	20.38 (29.48)	0.660
Echocardiography variables				
LAD (mm) mean (SD)	42.14 (5.97)	41.36 (5.59)	42.59 (6.21)	0.481
LAS (cm2) mean (SD)	22.33 (4.28)	21.59 (4.88)	22.87 (3.78)	0.379

AF: atrial fibrillation; AFL: atrial typical flutter; AT: atrial tachycardia; BMI: body mass index; HM: 24h-holter monitoring; ILR: internal loop recorder; LA: left atrium; LAD: left atrium diameter; LAS: left atrium surface; LVEF: left ventricle ejection fraction; LVH: left ventricle hypertrophy; SV: supraventricular.

	Total population (n = 70)	Without AFL (n = 22)	With AFL (n = 48)	p-value
LA dilatation	45 (64.3%)	18 (81.8%)	27 (56.3%)	0.059
LVEF (%) mean (SD)	54.89 (12.52)	58.95 (13.13)	52.59 (11.71)	0.058
LVEF < 55%	26 (37.1%)	8 (36.4%)	18 (37.5%)	1.000
Electrophysiological variables				
AH interval (msec) mean (SD)	-	-	115.59 (32.53)	-
HV interval (msec) mean (SD)	-	-	51.77 (8.40)	-
PR interval (msec) mean (SD)	194.63 (43.67)	205.10 (41.08)	190.27 (44.38)	0.239
QRS duration (msec) mean (SD)	113.91 (29.33)	117.35 (38.03)	112.48 (25.19)	0.898
SV ectopy > 0.2% at 24h-HM	23 (32.8%)	10 (45.4%)	13 (27%)	0.172
Atrial Tachycardia at 24h-HM	25 (35.7%)	9 (40.9%)	16 (33.3%)	0.597
SV ectopy > 0.2% or AT at 24h-HM	36 (51.4%)	13 (59.1%)	23(47.9%)	0.446
AT at ILR	16 (22.8%)	4 (18.2%)	12 (25%)	0.760
Bradycardia at ILR	15 (21.4%)	5 (22.7%)	10 (20.8%)	1.000

AF: atrial fibrillation; AFL: atrial typical flutter; AT: atrial tachycardia; BMI: body mass index; HM: 24h-holter monitoring; ILR: internal loop recorder; LA: left atrium; LAD: left atrium diameter; LAS: left atrium surface; LVEF: left ventricle ejection fraction; LVH: left ventricle hypertrophy; SV: supraventricular.

Typical atrial flutter is the strongest predictor for new onset AF

When examining the entire cohort, the only two variables associated with new onset AF were the history of previously ablated typical AFL and the presence of SVE. Interestingly CHA2DS2-VASC score was not associated to new onset AF (3.3 ± 1.6 in patients without AF at follow-up vs 3.1 ± 2 in patients with AF at follow-up; p = 0.61). Among patients with AFL, 56.3% developed new onset AF, vs 22.7% of patients without AFL (p = 0.011). Concerning atrial ectopy, among patients with SVE 58.3% developed new onset AF, vs 32.4% of patients without SVE (p = 0.039). Survival analyses demonstrated AFL as the only predictor for new onset AF at median follow-up of 12 months (Q1-Q3: 4–19 months; HR: 3.82; 95% CI: 1.46–10.03; p = 0.006). Multivariate analyses, including PACE calculator score, LA enlargement, and hypertension confirmed AFL as the only predictor (see Table 2).

Table 2
Multivariate analysis of predictors for AF in the entire cohort

	HR (95% IC	p-value
PACE calculator	1.02 [1.00;1.03]	0.076
Hypertension	1.17 [0.49;2.78]	0.728
LA dilatation	1.44 [0.65;3.21]	0.370
AFL	5.96 [2.01;17.73]	0.001
AF: atrial fibrillation; AFL: atrial typical flutter; LA: left atrium		

Figure 2 shows the survival curve for freedom from AF incidence in relation to the presence of AFL.

Predictors for new onset AF in patients with previous AFL

Focusing only on patients with previous AFL ablation, Table 3 shows the characteristics of patients with vs without new onset AF at follow-up. Interestingly SVE remains as the only variable associated with AF in this subgroup of patients (73.9% of patients with SVE vs 26.1% without SVE; p = 0.023).

Table 3
Characteristics of patients who underwent AFL ablation who developed new onset AF

	Total AFL group (n = 48)	No AF (n = 21)	New onset AF (n = 27)	p-value
Clinical variables				
BMI (kg/m2) mean (SD)	30.18 (5.99)	31.84 (5.94)	29.04 (5.91)	0.300
Glom. F (ml/min) mean (SD)	69.54 (19.10)	70.30 (16.34)	68.96 (21.29)	0.790
Hemoglobin (mg/dL) mean (SD)	13.99 (1.82)	14.21 (1.94)	13.82 (1.74)	0.379
Hypertension	34 (70.8%)	14 (66.7%)	20 (74.1%)	0.750
Tobacco use	24 (50%)	10 (47.6%)	14 (51.8%)	0.482
Diabetes mellitus	16 (33.3%)	6 (28.6%)	10 (37%)	0.758
Dyslipidemia	22 (45.8%)	12 (57.1%)	10 (37%)	0.244
Ischemic disease	10 (20.8%)	3 (14.3%)	7 (25.9%)	0.478
Valvular disease	2 (4.2%)	1 (4.7%)	1 (3.7%)	1
Stroke	1 (2.1%)	0 (0%)	1 (3.7%)	1
CHA2DS2-VASC	2.7 (1.6)	2.7 (1.5)	2.7 (1.7)	1
PACE Calc (% at 3 y) mean (SD)	20.09 (19.30)	14.73 (14.28)	24.41 (21.88)	0.104
Polysomnography variables				
Snorer	21 (43.7%)	9 (42.9%)	12 (44.4%)	1
Epworth mean (SD)	8.92 (4.45)	7.58 (4.12)	10.07 (4.55)	0.165
IAH mean (SD)	34.60 (20.34)	32.83 (14.89)	36.01 (24.28)	0.961
CT90% mean (SD)	20.38 (29.48)	33.88 (37.70)	8.80 (12.50)	0.060
Echocardiography variables				
LAD (mm) mean (SD)	42.59 (6.21)	42.40 (5.96)	42.73 (6.50)	0.817
LAS (cm2) mean (SD)	22.87 (3.78)	23.17 (4.43)	22.67 (3.40)	0.933
LA dilatation	27 (56.2%)	10 (47.6%)	17 (63%)	0.382

AF: atrial fibrillation; AFL: atrial typical flutter; AT: atrial tachycardia; BMI: body mass index; HM: 24h-holter monitoring; LA: left atrium; LAD: left atrium diameter; LAS: left atrium surface; LVEF: left ventricle ejection fraction; LVH: left ventricle hypertrophy; SV: supraventricular.

	Total AFL group (n = 48)	No AF (n = 21)	New onset AF (n = 27)	p-value
LVEF (%) mean (SD)	52.59 (11.71)	52.63 (14.23)	52.57 (9.94)	0.875
LVEF < 55%	18 (37.5%)	8 (38.1%)	10 (37%)	1
LVH	15 (31.2%)	7 (33.3%)	8 (29.6%)	1
Electrical variables				
AH interval (msec) mean (SD)	115.59 (32.53)	112.00 (21.84)	117.55 (37.98)	1
HV interval (msec) mean (SD)	51.77 (8.40)	48.00 (5.25)	54.13 (9.25)	0.092
PR interval (msec) mean (SD)	180.27 (44.38)	177.48 (57.02)	184.67 (31.39)	0.589
QRS duration (msec) mean (SD)	112.48 (25.19)	112.14 (24.93)	112.74 (25.86)	0.975
SV ectopy > 02% at 24h-HM	13 (27.1%)	5 (23.8%)	8 (29.6%)	0.750
Atrial tachycardia at 24h-HM	16 (33.3%)	4 (19%)	12 (44.4%)	0.075
SV ectopy > 0,2% or AT at 24h-HM	23 (47.9%)	6 (28.6%)	17 (63%)	0.023

AF: atrial fibrillation; AFL: atrial typical flutter; AT: atrial tachycardia; BMI: body mass index; HM: 24h-holter monitoring; LA: left atrium; LAD: left atrium diameter; LAS: left atrium surface; LVEF: left ventricle ejection fraction; LVH: left ventricle hypertrophy; SV: supraventricular.

Univariate analyses demonstrated a clear trend, although not significant, for SVE (HR 2.14, 95% CI: 0.98–4.68; p = 0.057). Among continuous variables the HV interval was the only predictor for new onset AF, with a HR 1.08 (95% CI: 1.01–1.16; p = 0.026). The PACE calculator revealed a trend towards predicting AF, (HR 1.02, 95% CI: 1-1.03; p = 0.1).

Given the fact that SVE is included in the PACE calculator and that SVE and HV interval showed a limited discrimination potential as continuous variables, we carried out a new analysis using the PACE calculator and HV interval as categorical variables (Table 4). Multivariate analyses showed that a PACE calculator score of ≥30% predicted the occurrence of new onset AF at a median follow-up of 12 months (Q1-Q3: 4–19 months), with a HR of 6.9 (95% CI: 1.71–27.91; p = 0.007) and HV interval of ≥55msec predicted the occurrence of new onset AF with a HR of 11.86 (95% CI: 2.57–54.8; p = 0.002). Interestingly LA dilatation did not predict AF incidence in our population. Figure 3shows survival curves for freedom from AF incidence related to the PACE calculator score and HV interval, respectively, in patients with previously ablated AFL.

Table 4
Multivariate analysis of predictors for AF in patients who had AFL ablation

	HR (95% IC	p-value
PACE calculator ≥ 30	6,9 [1,71;27,91]	0.007
HV interval > 55	11,86 [2,57;54,83]	0.002
Hypertension	2,27 [0,67;7,73]	0.191
LVH	0,66 [0,24;1,82]	0.421
LA dilatation	0,47 [0,14;1,58]	0.220
Ischemic disease	0,43 [0,1;1,89]	0.262
Glom. F. (ml/min)	1,01 [0,99;1,04]	0.345
QRS duration (msec)	0,99 [0,97;1,02]	0.535
Hemoglobin (mg/dL)	0,88 [0,67;1,16]	0.371
AF: atrial fibrillation; AFL: atrial typical flutter; LA: left atrium; LVH: left ventricle hypertrophy		

Predicting high-risk patients

We analyzed the added value of considering the PACE calculator score and/or HV interval in order to better stratify the risk for new onset AF in patients undergoing an AFL ablation procedure. Concerning the PACE calculator, a score of ≥30% predicted the incidence of new onset AF during follow-up with a specificity of 90.5%, a sensitivity of 38.5%, a positive predictive value (PPV) of 83.3% and a negative predictive value (NPV) of 54.3%. Regarding the HV interval, a value of ≥55 msec predicted the incidence of new onset AF during the follow-up with a specificity of 88.9%, a sensitivity of 62.5%, a positive predictive value (PPV) of 88.2% and a negative predictive value (NPV) of 64%. Therefore if the PACE score was ≥ 30 or the HV was ≥ 55msec, the probability of developing AF at a median of 12 months follow-up was greater than 83% and 88%, respectively. Figure 4 shows area under ROC curve to predict new onset AF in patients with AF with PACE calculator score ≥ 30 or with HV interval ≥ 55msec, respectively. Finally when combining both variables, the NPV of having a PACE calculator score of < 30 and an HV interval of < 55msec was 75% (95% CI: 50.9%-91.3%).

Discussion

Typical flutter as a risk factor for AF

New onset AF can be observed in a high proportion of patients after an AFL ablation [4–13] but studies addressing this issue are retrospective and most of them are based on 24-h holter monitoring, and it is well known that AF detection increases with more frequent and continuous monitoring [8,9]. We prospectively included seventy patients and monitored them continuously with ILR or CDAL. It was expected that the patients with AFL had less comorbidities and lower PACE scores than the patients

without AFL, as they were enrolled solely for a history of AFL undergoing ablation. We found that the presence of AFL was associated with a much more increased risk that we expected for developing new onset AF when compared to other known clinical risk factors (56.3% with AFL vs 22.7% without AFL, p = 0.011). Atrial flutter was the only independent predictor for new onset AF at median follow-up of 12 months (Q1-Q3: 4–19 months; HR: 3.82; 95% CI: 1.46–10.03; p = 0.006) follow-up, with an incidence of more than 56%. Despite several prior studies demonstrating a high incidence of new onset AF after AFL ablation, the findings of this study are unique in that it is the first prospective study evaluating clinical and noninvasive variables, as well as invasive data from electrophysiological studies. This data confirms the link between AFL and development of new onset AF, but suggests it is even stronger than previously believed, probably due to the presence of advanced substrate for AF. It is likely that the high incidence of new onset AF in this study is due to both the high risk profile of patients included (average CHA2DS2-VASC score of 3.2) and the use of continuous long-term monitoring with ILR or CDAL in all patients.

Very high-risk patients

Several variables have been described to predict new onset AF occurrence after AFL ablation. A large retrospective study included patients with and without previous AF [6], and correlated LA enlargement with the occurrence of new onset AF, but with a limited HR of 1.058 [7]. We did not find any association between LA enlargement and new onset AF but the limited size of our population could have influenced the results. The presence of advanced interatrial block, which is linked to LA enlargement [10], has been also described as a predictor for new onset AF in patients with AFL. This parameter is useful since it can be observed in a 12-lead ECG. Unfortunately we did not collect this information. Instead we collected the PR interval, which takes part in the PACE calculator, and other surface and intracardiac electrophysiological parameters such as QRS duration, AH interval and HV interval. We found a PACE calculator score of ≥30% and/or an HV interval of ≥55 msec to be the only, but strong predictors for new onset AF at follow-up. This finding reinforces the PACE calculator as a useful tool to predict AF in the general population as well as to further risk stratify patients after AFL ablation, since it behaved as independent predictor, providing additional and complimentary information. Of importance the PACE calculator includes significant atrial ectopy as a predictor, which was associated to new onset AF at follow-up in the general population. We could not find any other predictor, including left atrium dilatation or OSAS. Finally we found that both a high PACE calculator score and/or a long HV interval are very specific predictors for new onset AF in this subset of patients, with a very good PPV. Concerning our findings with the HV interval, this parameter has been previously correlated inversely with the left ventricular ejection fraction in patients with structural heart disease [19], and an HV interval of ≥ 55 msec has also been associated to atrial arrhythmias [20]. Given that patients with isolated AFL develop not only new onset AF but also stroke [21] at a higher rate than general population we believe that both variables could be of help in the decision for rigorous monitoring for AF and even in the decision for long-term anticoagulation in determinate cases: if either the PACE score is ≥ 30 or the HV interval is ≥ 55msec, the probability of developing AF at a median of 12 month follow-up is greater than 83% and this would favor the decision of not to stop anticoagulation after AFL ablation; on the other hand if both, the PACE

calculator score and the HV interval, are below those limits, the probability maintaining sinus rhythm is 75%, indicating that discontinuation of anticoagulation would be probably safe.

Interestingly, some centers have performed prophylactic pulmonary vein isolation in patients with AFL but without documented AF [22,23]. Results have revealed a significant reduction in recurrent atrial arrhythmias. From our point of view such a strategy could be of use in individualized high-risk cases, namely young patients with AFL with a high PACE calculator score or long HV interval, but this should be assessed in a prospective randomized study.

Limitations

It is likely that the high incidence of new onset AF in this study is due to both the high risk profile of patients included (average CHA2DS2-VASC score of 3.2) and the use of continuous long-term monitoring with ILR or CDAL in all patients. This study may have been limited by the small sample size, which may have accounted for the lack of predictive value of left atrial dilation or sleep apnea. Importantly despite this inconvenience we have been able to reach the two most relevant independent predictors for new onset AF in this setting of previous AFL ablation. This should be complemented with further research of predictors in a more extensive sample size.

Conclusions

In summary, we find that AFL is the most important predictor for new onset AF in a prospective study evaluating comprehensive clinical, noninvasive and invasive electrophysiological parameters, with long-term continuous cardiac monitoring. Patients with AFL have even greater risk for AF than patients with significantly increased comorbidities, traditional risk factors for AF, and higher PACE calculator score. Additionally, in patients who undergo AFL ablation, a high PACE score or long HV interval predicts very high risk for developing AF. These patients should be considered for rigorous monitoring for AF or even for empiric long-term anticoagulation in determinate cases. A large prospective randomized trial should be performed in order to confirm these findings.

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Figures

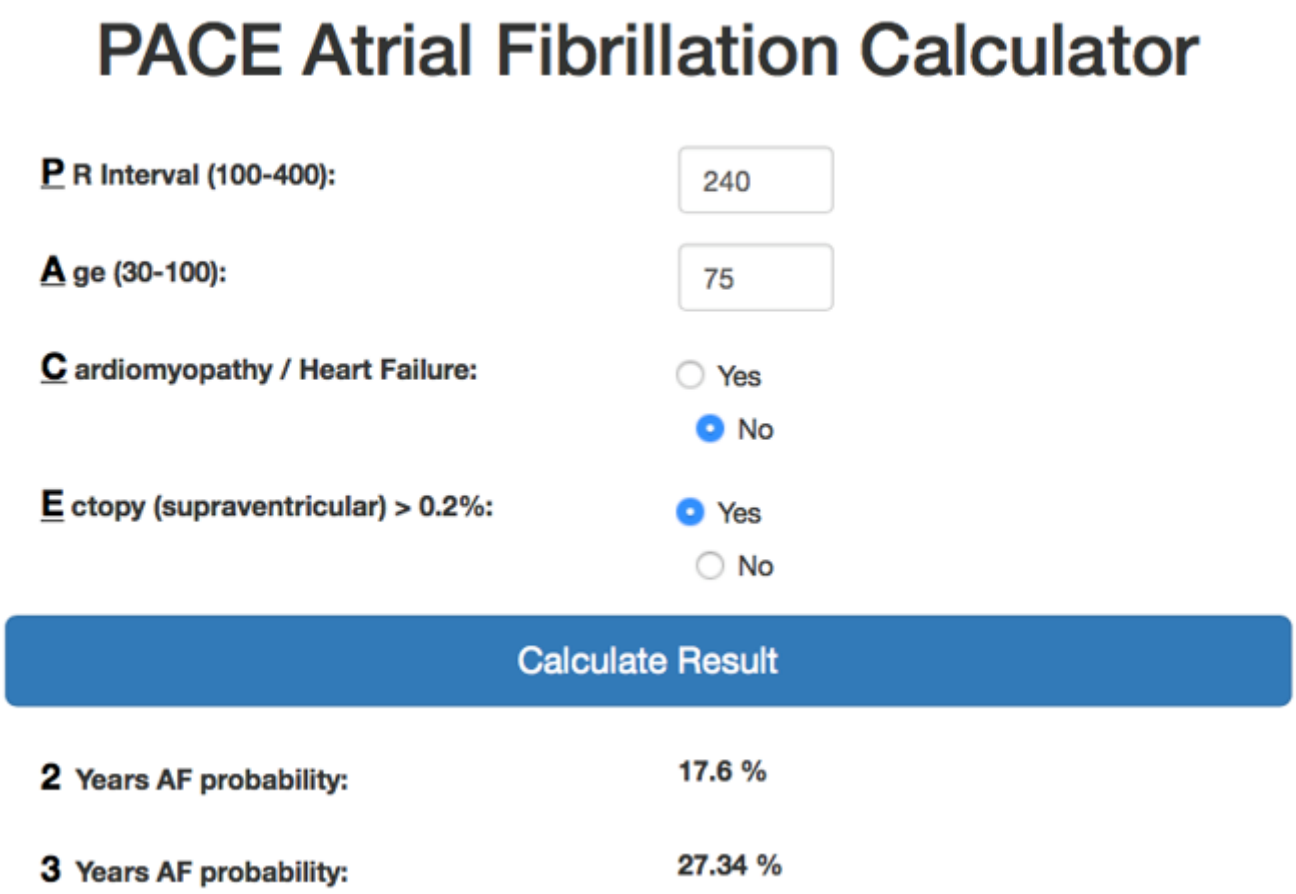

Figure 1

Example of the 2 and 3 years new onset AF risk calculation by means of PACE calculator from the website.

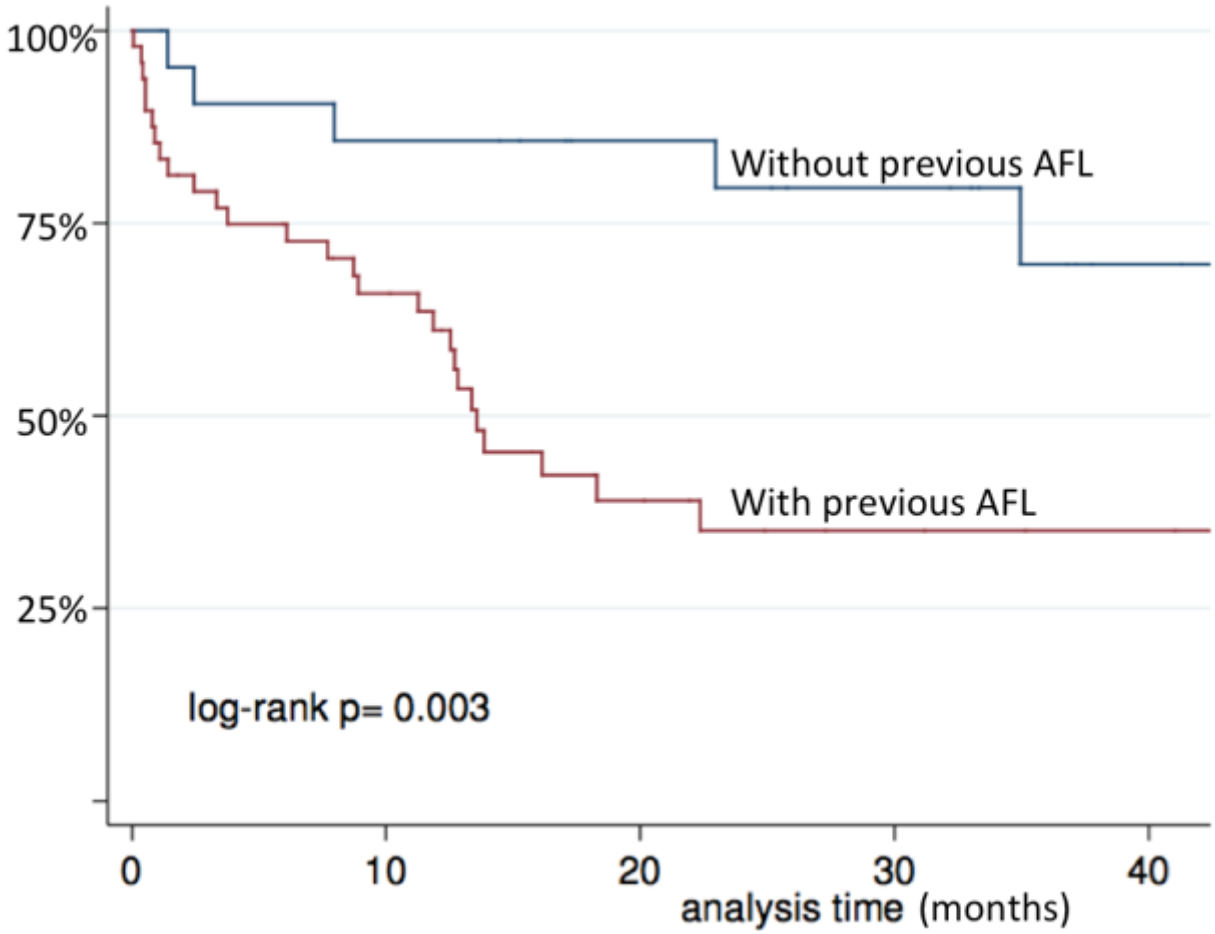

Figure 2

Freedom from AF depending on the presence of previous AFL Figure displays survival analyses for freedom from AF incidence depending on the presence of previous AFL. Blue and red lines show survival for patients without and with previous AFL, respectively. AF: atrial fibrillation; AFL: typical atrial flutter

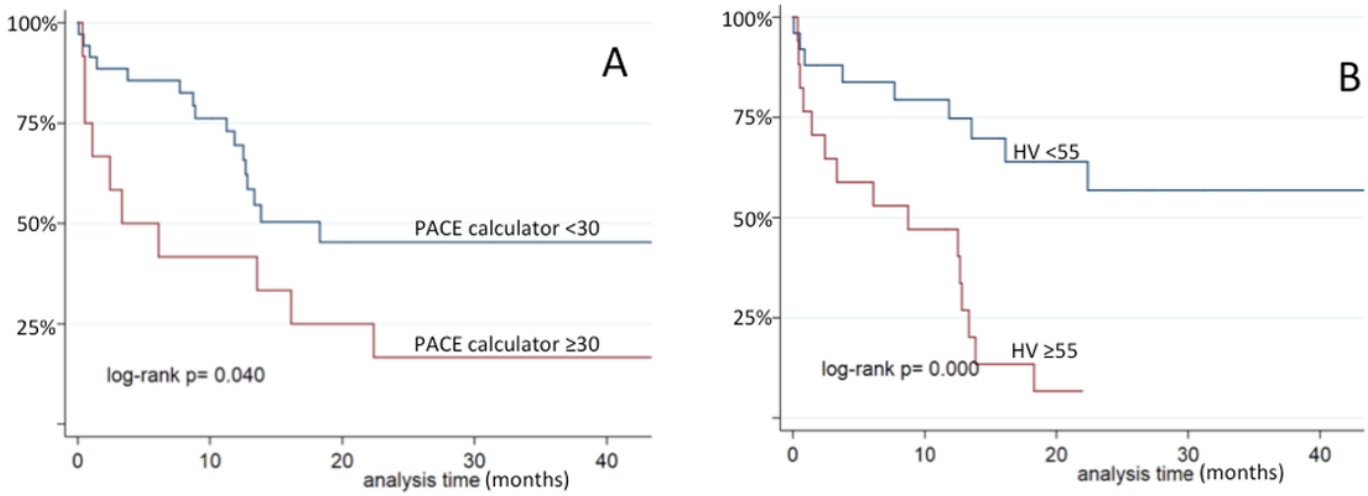

Figure 3

Survival analyses for freedom from AF depending on PACE calculator score and HV interval in patients with previous AFL Figure shows survival analyses for freedom from AF incidence depending on PACE calculator score (A) and depending on HV interval (B) in patients with previously ablated AFL. AF: atrial fibrillation; AFL: typical atrial flutter

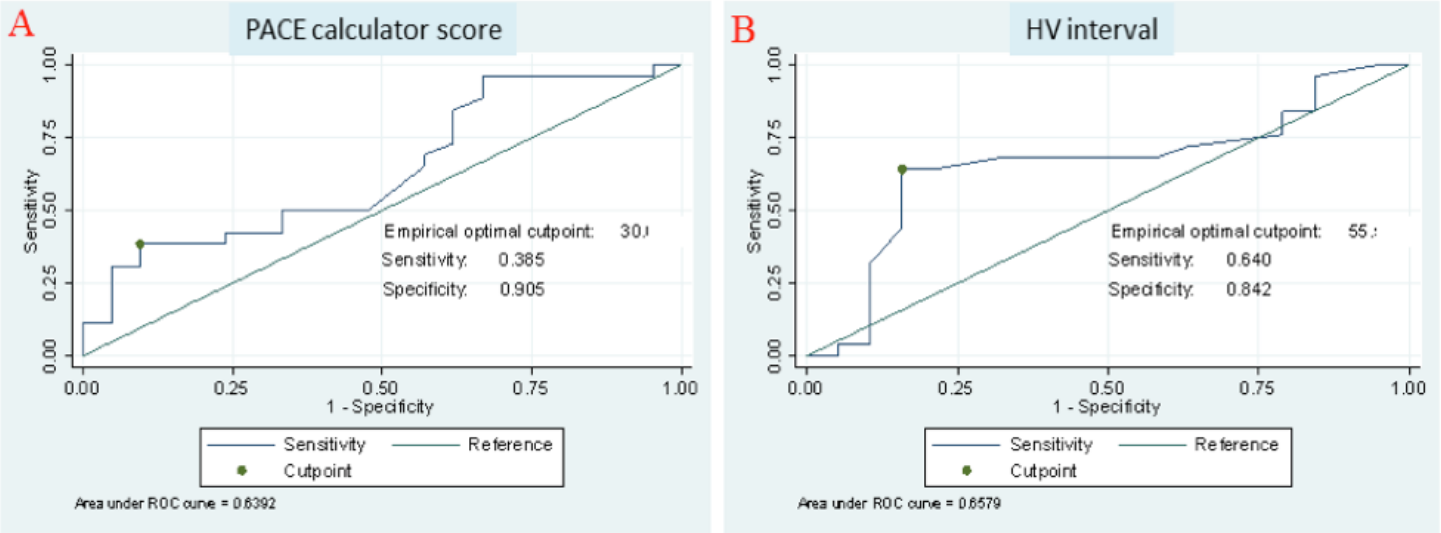

Figure 4

Area under ROC curve to predict new onset AF in patients with AFL Figure shows area under ROC curve for a PACE calculator score ≥30 (A) and for an HV interval ≥55msec (B) to predict new onset AF in patients with AFL. AF: atrial fibrillation; AFL: typical atrial flutter