ORIGINAL ARTICLE

Catheter ablation of the cavotricuspid isthmus in patients with atrial flutter: predictors of long-term outcomes

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KEY WORDS
ablation, atrial flutter, outcome, predictors

ABSTRACT

BACKGROUND Predictors of long-term outcomes and an optimal catheter set for ablation of the cavotricuspid isthmus in patients with atrial flutter (AFL) are not well known.

AIMS This study aimed to identify predictors of clinical events following ablation.

METHODS We studied 741 patients (mean [SD] age, 62.2 [10.8] years; 248 women) who were followed for a mean (SD) time of 4.4 (2.7) years. The 2- versus 3-electrode approach and clinical predictors of clinical events during follow-up were analyzed.

RESULTS The 2-electrode approach was faster (mean [SD] time, 62.5 [30.3] vs 101.4 [51] min; P <0.001), associated with shorter fluoroscopy time (13.1 [9.3] vs 20.3 [12.4] min; P < 0.001), cost-effective (8.29 [2.82] vs 11.89 [2.51] units; P <0.001), and more effective (92.1% vs 86.1%; P = 0.012). The independent predictors of AFL recurrence were: calcium blocker use (hazard ratio [HR], 3.24; 95% CI, 1.64–6.4), mitral valve disease (HR, 1.82; 95% CI, 1.12–2.95), previous stroke and / or TIA (HR, 2.38; 95% CI, 1.21–4.65), pulmonary artery dilatation (HR, 3.94; 95% CI, 1.22–12.73), and previous pulmonary embolism (HR, 3.77; 95% CI, 1.14–12.43); of atrial fibrillation (AF): previous AF (HR, 6.054; 95% CI, 4.58–8), left atrial enlargement (HR, 1.43; 95% CI, 1.12–1.81), number of antiarrhythmic drugs used (HR, 1.16; 95% CI, 1.05–1.28), and mitral valve disease (HR, 1.28; 95% CI, 1.04–1.58); of pacemaker implantation: tachycardia-bradycardia syndrome (HR, 6.17; 95% CI, 3.16–12.05), previous second-/third-degree atrioventricular block (HR, 29.4; 95% CI, 7.37–117.28), centrally acting hypotensive drugs (HR, 29.55; 95% CI, 6.14–142.25), aortic dilatation or aneurysm (HR, 2.58; 95% CI, 1.06–6.3), a labile international normalized ratio (HR, 3.45; 95% CI, 1.72–6.93), left bundle branch block (HR, 4.7; 95% CI, 1.49–14.82), the shortest R-R interval during AFL (HR, 1.003; 95% CI, 1.001–1.005), previous cardiac surgery (HR, 2.69; 95% CI, 1.27–5.7), and aortic valve disease (HR, 2.22; 95% CI, 1.08–4.59).

CONCLUSIONS Ablation of cavotricuspid isthmus with a minimal number of electrodes is safe and effective. Specific predictors of clinical events during long-term follow-up can be determined.

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INTRODUCTION Cavotricuspid isthmus (CTI)–dependent atrial flutter (AFL) is one of the most common supraventricular tachyarrhythmias.[1] Catheter ablation for AFL is an effective method of treatment and has been successfully used for 30 years.[2] Some technical and clinical issues have not been resolved yet. The aim of this study was to compare safety, efficacy, and cost-effectiveness of 2-electrode (2C) versus 3-electrode (3C) approach and to identify clinical predictors of long-term ablation failure, occurrence of atrial fibrillation (AF), and the need for pacemaker implantation.

WHAT'S NEW?

The 2-catheter approach for ablation of typical atrial flutter is at least as effective and safe as the conventional 3-electrode approach. Easily accessible, simple clinical and demographic parameters are useful for preprocedural identification of patients at risk of atrial flutter recurrence, atrial fibrillation, or need for pacemaker implantation following ablation of typical atrial flutter.

METHODS This study was a retrospective analysis of consecutive 714 patients with AFL who underwent CTI ablation between 2001 and 2016 in 2 electrophysiology centers and fulfilled the following inclusion criteria: 1) documented isthmus-dependent AFL during electrophysiology examination or standard 12-lead electrocardiography (ECG) documentation of typical AFL; 2) no previous AFL ablation; and 3) written informed consent for using demographic, procedural, and clinical characteristics for research purposes and participation in the follow-up.

TABLE 1 Demographic and clinical characteristics of the study group

Parameter	Value
Age, y, mean (SD)	62.2 (10.8)
Female sex	248 (33.5)
Body mass index, kg/m^2, mean (SD)	29 (4.7)
Hypertension	519 (70)
Coronary artery disease	226 (30.5)
Heart failure	240 (32.4)
Moderate-to-severe valvular heart disease	288 (38.9)
Left atrial enlargement	576 (78)
Right atrial enlargement	357 (48)
Left ventricular ejection fraction, %, mean (SD)	54.6 (10.9)
Diabetes	127 (17.1)
Chronic kidney disease	41 (5.5)
Chronic obstructive pulmonary disease	82 (11.1)
Obstructive sleep apnea	87 (11.7)
History of atrial flutter, mo, median (IQR)	34 (15–60)
Previous cardioversion, n, median (IQR)	2 (1–4)
Ineffective antiarrhythmic drugs, n, mean (SD)	2.1 (1)
History of concomitant atrial fibrillation	489 (66)
History of stroke / transient ischemic attack	49 (6.6)
Implanted pacemaker or cardioverter-defibrillator	71 (9.6)
Tachycardia-bradycardia or sick sinus syndrome	202 (27.3)
Left bundle branch block on standard ECG	38 (5.1)
History of cardiac surgery	53 (7.2)
Follow-up, y, mean (SD)	4.4 (2.7)

Data are presented as number (percentage) unless otherwise indicated.

Abbreviations: ECG, electrocardiography; IQR, interquartile range

Typical AFL on ECG was defined as the presence of regular flutter waves dominantly negative in the inferior leads (sawtooth pattern), with positive waves in lead V_1 (counterclockwise AFL) or as the presence of regular flutter waves dominantly positive in the inferior leads and negative in lead V_1 (clockwise AFL).[2,3] Electrocardiograms not fulfilling the above criteria were regarded as showing atypical AFL.

The study was approved by the local ethics committee. Exclusion criteria were as follows: lack of consent, previous ablation for AFL, and ablation of another arrhythmia at the same session.

Ablation procedure All procedures were performed on uninterrupted anticoagulation. In patients with ongoing AFL, entrainment was used to confirm that the CTI was a part of the arrhythmia circuit. If a patient arrived to an electrophysiology laboratory in sinus rhythm (SR), ablation was performed without induction of AFL if typical AFL was documented. In patients in whom ECG was inconclusive, induction of isthmus-dependent AFL was mandatory. The CTI involvement in the AFL circuit was confirmed by entrainment from the CTI during AFL and measuring the post-pacing interval, which should not exceed 30 ms compared with the AFL cycle length. The choice of electrodes was left at the operator's discretion. Two approaches were used. The 3C set included an ablation catheter, a diagnostic catheter introduced into the coronary sinus (CS), and a catheter placed along the tricuspid annulus (TA). The 2C approach involved ablation and a diagnostic electrode placed in the CS or along the TA. The catheter located at the TA was a HALO-like catheter or a standard diagnostic catheter.

Radiofrequency current was applied at a power of 50 to 60 Watts and temperature of 55 °C to 60 °C for nonirrigated catheters, and 30 to 40 Watts at an irrigation flow of 30 ml/min for irrigated catheters. The goal was to achieve bidirectional block in the CTI, confirmed by the presence of double potentials separated by more than 100 ms, differential pacing maneuver, and change in the activation sequence on the TA catheter. Pacing to reinduce AFL after achieving bidirectional block was not mandatory. The waiting time was 20 min.

Follow-up Patients were followed up in 2 centers participating in the study or cardiology departments close to the patient's place of living. Patients' data on follow-up clinical events and medical records were obtained from attending physicians. Visits were scheduled at 4 to 8 weeks, 6 months, and 12 months after ablation when standard ECG and a 24-hour ECG Holter examination were also performed. After a year, the visits were scheduled according to the attending physician's plan and the patient's needs. Patients

TABLE 2 Comparison of 2- and 3-electrode ablation

Parameter	2C group (n = 503)	3C group (n = 238)	*P* value
Procedure duration, min, mean (SD)	62.5 (30.3)	101.4 (51)	<0.001
Fluoroscopy time, min, mean (SD)	13.1 (9.3)	20.3 (12.4)	<0.001
Absorbed dose, mGy, median (IQR)	51 (24.6–131.2)	224.4 (136.2–358.7)	<0.001
Sheaths, n, mean (SD)	2.02 (0.14)	3.01 (0.11)	<0.001
Diagnostic electrodes, n, mean (SD)	1 (0)	2.01 (0.09)	<0.001
Cost of equipment, units[a], mean (SD)	8.29 (2.82)	11.89 (2.51)	<0.001
Cool-tip irrigated ablation electrode	30 (6)	12 (5)	0.61
4-mm ablation electrode	8 (1.6)	6 (2.5)	0.56
8-mm ablation electrode	465 (92.5)	220 (92.4)	0.99
Quadripolar CS electrode	35 (7)	0	<0.001
Decapolar CS electrode	205 (40.8)	235 (98.7)	<0.001
Quadripolar TA electrode	16 (3.2)	0	0.005
Decapolar TA electrode	75 (15)	5 (21)	<0.001
Duodecapolar TA electrode (HALO-like)	177 (35.2)	230 (96.7)	<0.001
Major hematoma, ↓hemoglobin >1 g/dl	1 (0.2)	2 (0.8)	0.51
Minor hematoma, ↓hemoglobin <1 g/dl	15 (3)	3 (1.3)	0.16
Arteriovenous fistula	–	2 (0.8)	0.19
Acute success[b]	446 (89)	209 (88)	0.74
Long-term success[c]	463 (92.1)	205 (86.1)	0.01
Follow-up duration, y, mean (SD)	3.7 (2.3)	5.93 (2.98)	<0.001

Data are presented as number (percentage) unless otherwise indicated.

a A single unit is equal to the cost of a diagnostic 4-pole electrode.
b Bidirectional block in the cavotricuspid isthmus
c No atrial flutter recurrence

Abbreviations: ↓, decrease; others, see TABLE 1

were encouraged to have ECG performed in case of symptoms suggesting cardiac arrhythmia. All patients were contacted by the investigator at the end of the follow-up to assess their status.

The analyzed endpoints included: 1) recurrence of typical AFL; 2) occurrence of AF which was defined as AF recorded on ECG or an episode lasting longer than 30 s on Holter ECG; and 3) pacemaker implantation.

Statistical analysis Study results were presented as mean (SD) if normally distributed or as median otherwise. To compare quantitative variables, the *t* test or the Wilcoxon test were used where appropriate. Quantitative parameters were compared using the χ^2 test. The Kaplan–Meier survival curves were calculated for the analyzed endpoints and compared using the log-rank test. To identify independent predictors associated with the analyzed endpoints, the Cox proportional hazard analysis with hazard ratio (HR) and CI calculations was performed. Based on the HR values, predictive models including independent variables were constructed. A *P* value less than 0.05 was considered significant.

RESULTS **Study group** A total of 797 patients with documented AFL underwent ablation of the CTI during the study. Of these, 56 met exclusion criteria. Finally, the study group consisted of 741 patients: 193 patients (26%) underwent ablation during ongoing CTI-dependent AFL, whereas 534 patients (72.1%) during SR. The remaining 14 (1.9%) presented other arrhythmias at the beginning of the procedure, which were cardioverted to SR or CTI-dependent AFL. Of these 548 (534 + 14) patients, 490 had typical AFL documented on ECG; however, 58 of them met ECG criteria for atypical AFL. In the latter group, AFL was induced before starting ablation and CTI involvement was confirmed. The mean (SD) follow-up duration was 4.4 (2.7) years. Detailed demographic and clinical characteristics of the study patients are presented in TABLE 1.

Comparison of 2- and 3-electrode ablation A total of 503 patients (68%) underwent 2C ablation, whereas 238 (32%)—3C ablation. Periprocedural parameters and efficacy of both approaches are compared in TABLE 2. Procedure duration, fluoroscopy time, the absorbed dose as well as the number and cost of tools were lower in the 2C than in the 3C group. There were no major complications, and the rate of local complications at the access site was low and similar in both groups. The acute procedural success was similar, whereas long-term success was slightly yet significantly higher in the 2C group (92% versus 86%; $P = 0.01$). Follow-up duration was significantly longer in the 3C group than in the 2C group.

Prediction of long-term efficacy The results of univariate and multivariate analyses are presented in TABLES 3 and 4. Eight parameters were associated with AFL recurrence (TABLE 3), whereas multivariate analysis identified the use of calcium channel blockers, moderate-to-severe mitral valve disease (MVD), prior stroke or TIA, pulmonary artery dilatation, and a history of pulmonary embolism as independent predictors of AFL recurrence (TABLE 4). The Kaplan–Meier curves for AFL recurrence in 3 study groups, divided according to the number of points calculated from the HR values, are shown in FIGURE 1. Patients who scored 0 to 2 points had a significantly lower probability of AFL recurrence compared with those with 3 or 4 points (P <0.001) and those with more than 4 points (P <0.001). Also, patients with 3 or 4 points showed a lower probability of AFL recurrence than those with more than 4 points ($P = 0.03$).

In a subgroup of 252 patients without known AF before AFL ablation, multivariate analysis showed that a history of pulmonary embolism and moderate-to-severe MVD were associated with AFL recurrence (HR, 14.5; 95% CI, 3.9–54; P <0.001 and HR, 3.2; 95% CI, 1.4–7.4; $P = 0.005$, respectively).

Prediction of atrial fibrillation occurrence after ablation for atrial flutter Fifteen parameters were associated with the occurrence of AF, whereas 4 parameters remained significant in multivariate analysis (presence of AF before AFL ablation, LA enlargement, number of antiarrhythmic drugs used before AFL ablation, and moderate-to-severe MVD). The Kaplan–Meier curves for AF occurrence in 3 study groups, divided according to the number of points calculated from the HR values, are depicted in FIGURE 2. Patients who scored 0 to 2 points showed a significantly lower probability of AF occurrence compared with patients with 3 or 4 points (P <0.001)

TABLE 3 Predictors of atrial flutter recurrence by univariate analysis

Parameter	Isthmus-dependent AFL recurrence (n = 73)	No AFL recurrence (n = 668)	*P* value
Prior stroke or transient ischemic attack	10 (13.7)	39 (5.8)	0.02
History of pulmonary embolism	3 (4.1)	5 (0.8)	0.04
Labile INR	15 (20.6)	77 (11.5)	0.03
Right atrial enlargement	45 (61.6)	312 (46.1)	0.02
Moderate-to-severe mitral valve disease	28 (38.4)	146 (21.9)	0.002
Moderate-to-severe tricuspid valve disease	29 (39.7)	180 (27)	0.02
Pulmonary artery dilatation	3 (4.1)	3 (0.5)	0.01
Use of calcium channel blockers before AFL ablation	10 (13.7)	25 (3.7)	<0.001

Data are presented as number (percentage).

Abbreviations: AFL, atrial flutter; INR, international normalized ratio

TABLE 4 Predictors of atrial flutter recurrence by multivariate analysis

Parameter	HR (95% CI)	Points	*P* value
Use of calcium channel blockers before AFL ablation	3.24 (1.64–6.4)	3.2	<0.001
Moderate-to-severe mitral valve disease	1.82 (1.12–2.95)	1.8	0.003
Prior stroke or transient ischemic attack	2.38 (1.21–4.65)	2.4	0.01
Pulmonary artery dilatation	3.94 (1.22–12.73)	3.9	0.02
History of pulmonary embolism	3.77 (1.14–12.43)	3.8	0.02

Abbreviations: HR, hazard ratio; others, see TABLE 3

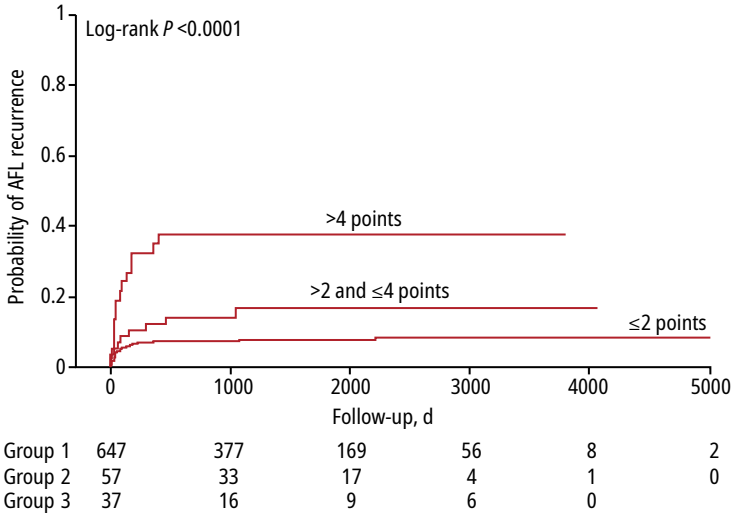

FIGURE 1 Kaplan–Meier curves for atrial flutter (AFL) recurrence according to the number of points scored in the risk stratification model

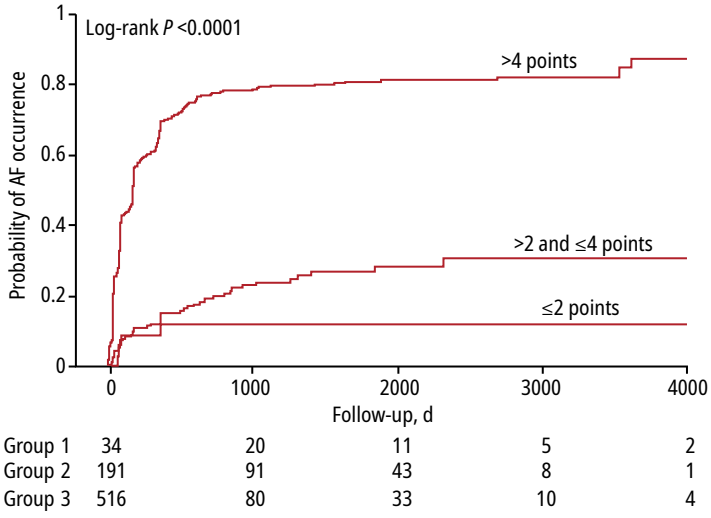

FIGURE 2 Kaplan–Meier curves for atrial fibrillation (AF) occurrence according to the number of points scored in the risk stratification model

and patients with more than 4 points (P <0.001). Also, patients with 3 or 4 points demonstrated a lower probability of AF occurrence than those with more than 4 points (P <0.001). There was no significant difference in AF occurrence between groups 2C and 3C (327 [65%] vs 137 [57.6%]; P = 0.05).

We conducted an analysis in 252 patients without known AF before the procedure. Only moderate-to-severe MVD proved to be a significant predictor of AF occurrence after AFL ablation (18/60 [30%] vs 34/192 [17.7%]; P = 0.04), however, it lost significance in the multivariate analysis (HR, 1.62; 95% CI, 0.93–2.82; P = 0.09). Detailed results are presented in TABLES 5 and 6.

Prediction of the need for pacemaker implantation after ablation for atrial flutter Sixteen parameters were significantly associated with the need for pacemaker implantation and 9 parameters remained significant in the multivariate analysis (tachycardia-bradycardia or sick sinus syndrome, a history of second- or third-degree atrioventricular block, centrally acting hypotensive drugs, aortic dilatation or aneurysm, a labile international normalized ratio (INR), left bundle branch block, a longer minimal R-R interval during AFL, a history of cardiac surgery, and aortic valve disease). The Kaplan–Meier curves for pacemaker implantation in 3 study groups, divided according to the number of points calculated from the HR values, are shown in FIGURE 3. Patients with 500 points or less were at a significantly lower risk of pacemaker implantation compared with those with 500 to 800 points (P <0.001) and those with more than 800 points (P <0.001). Patients with 500 to 800 points also showed a lower probability of pacemaker implantation than those who scored more than 800 points (P = 0.03).

Pacemaker implantation was less frequent in the 2C group than in the 3C group (22 [4.9%] vs 23 [10.2%]; P = 0.01). The median (interquartile range) time interval between ablation and pacemaker implantation was 94 (20–795) days (range, 1–2056). No implantation was performed because of iatrogenic conduction block. Detailed findings are presented in TABLES 7 and 8.

DISCUSSION

The present study showed that: 1) the use of a limited number of electrodes for ablation of the CTI in patients with AFL is at least as effective and safe as the multicatheter approach as well as more cost-effective than the latter; and 2) there are parameters that can be used to predict long-term patient outcomes.

Comparison of 2- and 3-catheter ablation Although the 2C approach is commonly used in clinical practice, the 3C approach is still advocated in the literature[3] and there are no studies comparing these 2 approaches. Studies that compared multicatheter versus minimal catheter strategies in patients with various supraventricular tachycardias showed that reducing the number of catheters is safe and effective.[4-6] The only study that addressed this issue in a subgroup undergoing AFL ablation showed that the minimal approach is safe, effective, cost-effective, and associated with the procedure time reduced by 25 minutes.[7] Our results substantiate these findings. The fact that the 2C approach turned out to be more effective than the 3C approach at long-term follow-up may be explained by the differences in the follow-up duration, which was longer in the 3C group.

Prediction of long-term efficacy All parameters that predicted the ablation outcome in our study are easily accessible from the patient's

TABLE 5 Predictors of atrial fibrillation occurrence by univariate analysis

Parameter	AF after AFL ablation (n = 464)	No AF after AFL ablation (n = 277)	*P* value
Female sex	179 (38.6)	69 (24.9)	<0.001
Left atrial enlargement	376 (81)	200 (72.2)	0.01
Moderate-to-severe mitral valve disease	125 (26.9)	49 (17.7)	0.004
EHRA class >I	452 (97.4)	258 (93.1)	0.005
NYHA class, median (IQR)	0 (0–1)	0 (0–1)	0.04
Concomitant AF	404 (87.1)	85 (30.7)	<0.001
Concomitant atrial tachycardia / atypical AFL	81 (17.5)	21 (7.6)	<0.001
Frequent supraventricular ectopic beats on Holter ECG, >200/24 hrs	75 (16.2)	30 (10.8)	0.04
Use of propafenone	269 (58)	93 (33.6)	<0.001
Use of amiodarone	148 (31.9)	56 (20.2)	<0.001
Use of sotalol	183 (39.4)	72 (6)	<0.001
Ineffective antiarrhythmic drugs (including β-blockers and calcium channel blockers), n, mean (SD)	2.33 (0.91)	1.81 (0.93)	<0.001
Electrical cardioversion, n, median (IQR)	1 (0–2)	1 (0–2)	<0.001
Pharmacological cardioversion, n, median (IQR)	2 (0–3)	0 (0–2)	<0.001
Overall cardioversion, n, median (IQR)	3 (1–5)	1 (0–3)	<0.001

Data are presented as number (percentage) unless otherwise indicated.

Abbreviations: AF, atrial fibrillation; EHRA, European Heart Rhythm Association; NYHA, New York Heart Association; others, see TABLES 1 and 3

TABLE 6 Predictors of atrial fibrillation occurrence by multivariate analysis

Parameter	HR (95% CI)	Points	*P* value
Concomitant atrial fibrillation	6.054 (4.58–8)	6.1	<0.001
Left atrial enlargement	1.43 (1.12–1.81)	1.4	<0.001
Number of ineffective antiarrhythmic drugs	1.16 (1.05–1.28)	1.2	0.01
Moderate-to-severe mitral valve disease	1.28 (1.04–1.58)	1.3	0.02

Abbreviations: see TABLE 4

history and echocardiographic examination. Patients with more than 4 points according to our risk stratification model had a 4-fold higher probability of AFL recurrence than those with less than 2 points and 2-fold higher than the intermediate-risk group.

The majority of studies focused on the type of an ablation catheter rather than on the clinical predictors of ablation outcomes.[8] Studies that investigated various predictors of ablation outcomes showed that fluoroscopy time, adenosine-induced reconduction through the CTI, reduced left ventricular ejection fraction, right atrial enlargement, obesity, occurrence of AF after AFL ablation, use of amiodarone before ablation, and anatomical localization of the right coronary artery very close to the CTI were associated with AFL recurrence.[9-12]

In our study, the long-term efficacy of CTI ablation ranged between 86% and 92%. This is in line with other reports; however, a wider use of irrigated catheters with contact force measurements and bipolar ablation can improve efficacy.[13-15]

Calcium channel blockers slow conduction velocity through the CTI and may hamper identification of the true bidirectional block in the CTI.[16] In such situation, a functional block in the CTI may be taken as a true block. If ablation is terminated at this point, AFL may recur. In addition, it may be speculated that the use of these drugs before ablation identified patients in whom it was difficult to control the ventricular rate during AFL or undetected AF. Thus, they were prone to tachycardiomyopathy, which may decrease ablation efficacy.

Another parameter predicting AFL recurrence in our study—valvular disease—is a well-established risk factor. Both tricuspid and mitral valve disease were associated with AFL recurrence; however, only MVD remained an independent predictor. The mechanisms leading to AFL recurrences include atrial remodeling, making it difficult to achieve bidirectional block, as well as right atrial strain and enlargement, which promote reentrant arrhythmias.

The association between previous stroke or TIA and AFL recurrence is difficult to explain. One can speculate that these patients might also have had undetected concomitant AF, manifested by a thromboembolic event. Atrial fibrillation

TABLE 7 Predictors of pacemaker implantation by univariate analysis

Parameter	No need for pacemaker implantation (n = 625)	Pacemaker implanted after AFL ablation (n = 45)	*P* value
Female sex	193 (30.9)	23 (51.1)	0.01
Age, y, mean (SD)	61.13 (10.63)	67.36 (9.38)	<0.001
CHA_2DS_2-VASc, mean (SD)	2.22 (1.49)	2.87 (1.59)	0.01
HAS-BLED, mean (SD)	1.57 (1.03)	2.16 (0.98)	<0.001
Thyroid disease	100 (16)	15 (33.3)	0.003
Tachycardia-bradycardia syndrome or sick sinus syndrome	121 (19.4)	31 (68.9)	<0.001
History of second- or third-degree atrioventricular block	2 (0.3)	3 (6.7)	<0.001
Left bundle branch block on ECG	12 (1.9)	4 (8.9)	0.01
Previous cardiac surgery	38 (6.1)	10 (22.2)	<0.001
Aortic dilatation or aneurysm	27 (4.3)	8 (17.8)	<0.001
Labile INR	69 (11)	12 (26.7)	0.002
Aortic valve disease	73 (11.7)	17 (37.8)	<0.001
Centrally acting hypotensive drugs	1 (0.2)	2 (4.4)	0.003
Longest cycle length of the flutter wave on ECG, ms, mean (SD)	245.49 (23.33)	267.82 (51.01)	0.002
Shortest R-R interval during AFL, ms, mean (SD)	477.46 (105.63)	545.08 (142.43)	0.002
Maximal atrioventricular conduction during AFL[a], mean (SD)	2.02 (0.46)	2.24 (0.57)	0.004

Data are presented as number (percentage) unless otherwise indicated.

a The number of flutter waves divided by the number of QRS complexes

Abbreviations: see TABLES 1 and 3

TABLE 8 Predictors of pacemaker implantation by multivariate analysis

Parameter	HR (95% CI)	Points	*P* value
Tachycardia-bradycardia syndrome or sick sinus syndrome	6.17 (3.16–12.05)	6.2	<0.001
History of second- or third degree atrioventricular block	29.40 (7.37–117.28)	29.4	<0.001
Centrally acting hypotensive drugs	29.55 (6.14–142.25)	29.6	<0.001
Aortic dilatation or aneurysm	2.58 (1.06–6.3)	2.6	<0.001
Labile INR	3.45 (1.72–6.93)	3.5	<0.001
Left bundle branch block on ECG	4.7 (1.49–14.82)	4.7	<0.001
Shortest R-R interval during AFL	1.003 (1.001–1.005)	1	0.002
Previous cardiac surgery	2.69 (1.27–5.7)	2.7	0.01
Aortic valve disease	2.22 (1.08–4.59)	2.2	0.03

Abbreviations: see TABLES 3 and 4

causes left and right atrial remodeling, promoting AFL recurrences. In addition, patients with a history of a neurological episode often have an enhanced adrenergic tone, which may facilitate AFL recurrence.

Previous pulmonary embolism and subsequent pulmonary artery dilatation are known factors influencing right atrial pressure and diameter, which may hamper formation of bidirectional block as well as promote AFL recurrences during follow-up.

The abovementioned predictors of AFL ablation failure may be useful in deciding whether to perform the procedure, especially in patients

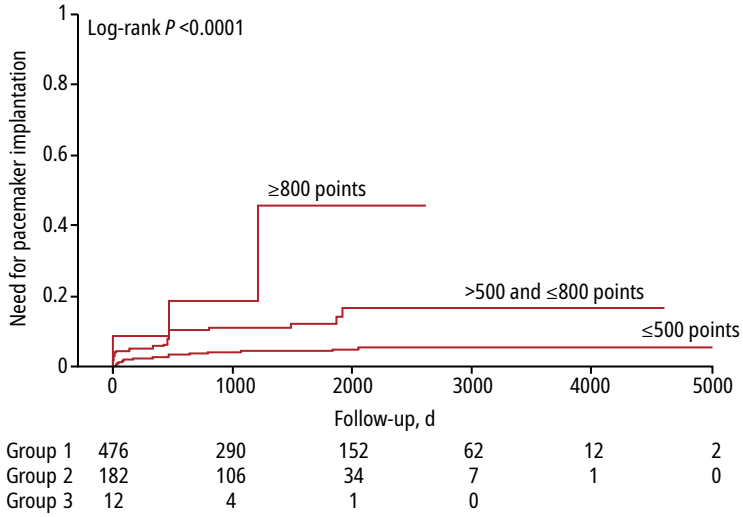

FIGURE 3 Kaplan–Meier curves for pacemaker implantation according to the number of points scored in the risk stratification model

with borderline indications for ablation, such as asymptomatic patients (class IIb according to the current guidelines).[17]

Prediction of atrial fibrillation occurrence after ablation for atrial flutter Atrial fibrillation occurring de novo or recurring despite AFL ablation is a significant clinical issue that affected 63% of our study patients. These patients continue to be symptomatic, remain at risk of thromboembolic events, and have an increased prevalence of heart failure and mortality.

Several studies addressed this issue[8,18-20] and showed that the prevalence of AF after AFL ablation may be as high as 80%. The most frequently encountered predictors of AF episodes are concomitant AF before ablation, left trial enlargement, MVD, and decreased left ventricular ejection fraction. The less frequently encountered predictors include younger age (<65 years), obstructive sleep apnea, chronic obstructive pulmonary disease, female sex, induction of AF during an electrophysiological study, obesity, endurance training, use of class I antiarrhythmic drugs and amiodarone, and echocardiographic parameters such as A-wave velocity.

Our study results are consistent with the previously published data. The only new independent parameter is the number of ineffective antiarrhythmic drugs used in the past. The higher the number, the greater the risk of AF occurrence after AFL ablation. This parameter probably identifies patients who had undetected AF before ablation and were treated for palpitations attributed to AFL. In all studies, concomitant AF detected before AFL ablation was the strongest predictor of AF episodes occurring after the procedure. This result is expected, since AFL ablation rarely cures AF. When patients with concomitant AF were excluded from the analysis, only MVD was more frequent in those with new-onset AF after AFL ablation, which suggests that ablation of both AFL and AF may be specifically indicated in such patients.

A preprocedural analysis of risk factors for AF may help in making the decision whether to perform AFL ablation only or AF+AFL ablation in first place, to plan follow-up to detect AF, and to continue or withhold anticoagulation. According to our risk stratification model, patients with more than 4 points were at almost 90% risk of AF occurrence after AFL ablation.

Prediction of the need for pacemaker implantation after atrial flutter ablation There is only a single study published that dealt with the prediction of the need for pacemaker implantation after AFL ablation.[21] It showed that a ventricular rate slower than or equal to 65 bpm during AFL and intraventricular conduction disturbances identified patients who needed pacemaker after AFL ablation. In our cohort, this parameter did not differentiate patients who required a pacemaker from those who did not, probably because we had only 4 patients with a heart rate slower than or equal to 65 bpm.

Such parameters as tachycardia-bradycardia or sick sinus syndrome diagnosed before AFL ablation, a history of atrioventricular block, left bundle branch block, or a longer minimal R-R interval during AFL are typical risk factors for symptomatic bradycardia and need for pacemaker implantation. Centrally acting hypotensive drugs (clonidine) may cause sinus bradycardia or atrioventricular block,[22] as they activate presynaptic α2-receptors and, thus, lower norepinephrine levels in cardiac tissue. Aortic aneurysm or dilatation and aortic valve disease have been shown to increase the incidence of atrioventricular block, especially when treated surgically or percutaneously,[23,24] because the atrioventricular node and the bundle of His are located close to the aortic valve. A labile INR may identify patients in whom thrombi migrating from the left atrium to the right coronary artery might have caused ischemia of the cardiac conduction system, leading to bradycardia. Also, a labile INR identifies patients with multiple comorbidities or those who are less adherent to prescribed medications.

The finding that more patients from the 3C group than from the 2C group underwent pacemaker implantation is difficult to explain and may be caused by longer follow-up in the former group.

In summary, preprocedural assessment may allow for better selection of candidates for ablation, especially asymptomatic or minimally symptomatic patients. In these patients, it is better to withhold AFL ablation rather than to perform the procedure that is likely to be effective, however, at a cost of pacemaker implantation.

Limitations This was a retrospective study with all limitations typical for such analysis. Although demographic, clinical, and procedural characteristics were collected uniformly from all patients at the time of ablation, there was no uniform follow-up scheme after 1 year and only 3 24-hour Holter ECG recordings were performed during the first year of follow-up. Thus, some important clinical parameters such as AF recurrences or asymptomatic tachyarrhythmias might have been missed. However, symptomatic AFL recurrences were detected accurately, because all such events led to the second AFL ablation. The need for pacemaker implantation was assessed properly, as it was based on the current number of implantations. Echocardiography examinations were performed by different investigators, which might have influenced the accuracy of results. The duration of follow-up was different in groups 2C and 3C, which also might have influenced the results. Furthermore, the types of diagnostic electrodes differed between the groups; however, ablation catheters were similar, thus, it should not influence the efficacy comparison. Finally, in the group of patients who had ablation performed during SR without confirmed CTI involvement in the AFL circuit, there might have been some individuals with non–CTI-dependent AFL. However, such possibility is low, because in patients with 12-lead ECG documentation typical of AFL, the CTI is part of the AFL circuit in over 90% of patients.[25]

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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REFERENCES

1 Granada J, Uribe W, Chyou PH, et al. Incidence and predictors of atrial flutter in the general population. J Am Coll Cardiol. 2000; 36: 2242-2246.

2 Katritsis DG, Boriani G, Cosio FG, et al. European Heart Rhythm Association (EHRA) consensus document on the management of supraventricular arrhythmias, endorsed by Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulación Cardiaca y Electrofisiologia (SOLAECE). Europace. 2017; 19: 465-511.

3 Shoei K, Huang S, Miller JM, et al. Catheter ablation of cardiac arrhythmias. In: Feld G, McGarry T, Olson N, et al, eds. Ablation of Cavotricuspid Isthmus – Dependent Atrial Flutters. 3rd ed. Oxford: Elsevier Ltd; 2014: 203-231.

4 Topilski I, Rogowski O, Glick A, et al. Radiofrequency ablation of atrioventricular nodal reentry tachycardia: a 14 year experience with 901 patients at the Tel Aviv Sourasky Medical Center. Isr Med Assoc J. 2006; 8: 455-459.

5 Wang L, Li J, Yao R, Song S. Simplified approach to radiofrequency catheter ablation of paroxysmal supraventricular tachycardia. Croat Med J. 2004; 45: 167-170.

6 Deutsch K, Śledź J, Mazij M, et al. Maximum voltage gradient technique for optimization of ablation for typical atrial flutter with zero-fluoroscopy approach. Medicine (Baltimore). 2017; 96: e6939.

7 Liew R, Baker V, Richmond L, et al. A randomized-controlled trial comparing conventional with minimal catheter approaches for the mapping and ablation of regular supraventricular tachycardias. Europace. 2009; 11: 1057-1064.

8 Pérez FJ, Schubert CM, Parvez B, et al. Long-term outcomes after catheter ablation of cavo-tricuspid isthmus dependent atrial flutter: a meta-analysis. Circ Arrhythm Electrophysiol. 2009; 2: 393-401.

9 Schmieder S, Ndrepepa G, Dong J, et al. Acute and long-term results of radiofrequency ablation of common atrial flutter and the influence of the right atrial isthmus ablation on the occurrence of atrial fibrillation. Eur Heart J. 2003; 24: 956-962.

10 Ventura M, Elvas L, Providência L. Previous therapy with amiodarone increases the recurrence rate in successfully ablated patients with isthmus-dependent atrial flutter. Rev Port Cardiol. 2004; 23: 1303-1311.

11 Klemm HU, Weber TF, Johnsen C, et al. Anatomical variations of the right coronary artery may be a source of difficult block and conduction recurrence in catheter ablation of common-type atrial flutter. Europace. 2010; 12: 1608-1615.

12 Morales G, Darrat YH, Lellouche N, et al. Use of adenosine to shorten the post ablation waiting period for cavotricuspid isthmus-dependent atrial flutter. J Cardiovasc Electrophysiol. 2017; 28: 876-881.

13 Kumar S, Morton JB, Halloran K, et al. Effect of respiration on catheter-tissue contact force during ablation of atrial arrhythmias. Heart Rhythm. 2012; 9: 1041-1047.e1.

14 Futyma P, Ciąpała K, Głuszczyk R, et al. Bipolar ablation of refractory atrial and ventricular arrhythmias: importance of temperature values of intracardiac return electrodes. J Cardiovasc Electrophysiol. 2019; 30: 1718-1726.

15 Orczykowski M, Borowiec K, Biernacka E, et al. Ablation of atrial tachyarrhythmias late after surgical correction of tetralogy of Fallot: long-term follow-up. Kardiol Pol. 2018; 76: 1097-1105.

16 Morita N, Kobayashi Y, Iwasaki YK, et al. Pronounced effect of procainamide on clockwise right atrial isthmus conduction compared with counterclockwise conduction: possible mechanism of the greater incidence of common atrial flutter during antiarrhythmic therapy. J Cardiovasc Electrophysiol. 2002; 13: 212-222.

17 Page RL, Joglar JA, Caldwell MA, et al. 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm. 2016; 13: 136-221.

18 Voight J, Akkaya M, Somasundaram P, et al. Risk of new-onset atrial fibrillation and stroke after radiofrequency ablation of isolated, typical atrial flutter. Heart Rhythm. 2014; 11: 1884-1889.

19 Seara JG, Roubin SR, Gude Sampedro F, et al. Risk of atrial fibrillation, stroke, and death after radiofrequency catheter ablation of typical atrial flutter. Clin Res Cardiol. 2014; 103: 543-552.

20 Brembilla-Perrot B, Girerd N, Sellal JM, et al. Risk of atrial fibrillation after atrial flutter ablation: impact of AF history, gender, and antiarrhythmic drug medication. J Cardiovasc Electrophysiol. 2014; 25: 813-820.

21 Rodríguez-Mañero M, González-Melchor L, Ballesteros G, et al. Risk of pacemaker implantation after uneventful successful cavotricuspid isthmus radiofrequency ablation in patients with common atrial flutter. Int J Cardiol. 2016; 202: 285-288.

22 Isbister GK, Heppell SP, Page CB, Ryan NM. Adult clonidine overdose: prolonged bradycardia and central nervous system depression, but not severe toxicity. Clin Toxicol (Phila). 2017; 55: 187-192.

23 Rampal U, Vasudev R, Bikkina M, Shamoon F. Complete heart block as an initial presentation of aortic dissection. Indian Heart J. 2016; 68: 386-388.

24 Erkapic D, De Rosa S, Kelava A, et al. Risk for permanent pacemaker after transcatheter aortic valve implantation: a comprehensive analysis of the literature. J Cardiovasc Electrophysiol. 2012; 23: 391-397.

25 Barbato G, Carinci V, Tomasi C, et al. Is electrocardiography a reliable tool for identifying patients with isthmus-dependent atrial flutter? Europace 2009; 11: 1071-1076.