Long-term progression from paroxysmal to permanent atrial fibrillation following transcatheter ablation in a large single-center experience

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BACKGROUND The natural history of atrial fibrillation (AF) is characterized by gradual increase in duration and frequency of relapses until a definitive shift to permanent AF. Heart disease and comorbidities modulate AF progression. However, to date the influence of catheter ablation on AF evolution has rarely been investigated.

OBJECTIVE The purpose of this study was to identify long-term predictors of AF progression in a large cohort of patients undergoing AF transcatheter ablation (AFTCA).

METHODS A total of 889 patients (mean age 57 ± 11 years; 53.3% paroxysmal AF, 40.5% persistent AF, 6.2% long-standing AF) underwent AFTCA. All patients underwent pulmonary vein isolation, with linear lesions and complex fractionated atrial electrogram ablation reserved for patients with persistent/long-standing AF and/or confirmed structural heart disease.

RESULTS After median follow-up of 64 months (range 41–84 years), AF progression despite AFTCA occurred in 57 cases (6.4%). However, AF progression was much more pronounced in patients with persistent (10%) or long-standing persistent AF (14.6%) than in those with paroxysmal AF (2.7%, $P < .001$). Furthermore, AF progression was more frequently reported in patients who presented with underlying comorbidities/cardiomyopathies (9.1%) than in those who presented with lone AF (29.9%, $P < .001$). At multivariate analysis, comorbidities/cardiomyopathies and baseline persistent/long-standing AF proved to be independent predictors of progression (odds ratio 11.3, 95% confidence interval 2.6–48.0, $P < .001$, and odds ratio 1.6, 95% confidence interval 1.2–2.1, $P < .001$, respectively).

CONCLUSION The presence of comorbidities/cardiomyopathies and persistent/long-standing AF seem to predict AF progression in patients undergoing AFTCA. Performing AFTCA in the paroxysmal phase of the arrhythmia may reduce progression of AF to its permanent form.

KEYWORDS Atrial fibrillation; Transcatheter ablation; Long-term progression; Permanent atrial fibrillation

ABBREVIATIONS AF = atrial fibrillation; **AFTCA** = atrial fibrillation transcatheter ablation; **IQR** = interquartile range; **PVI** = antral pulmonary vein isolation

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Introduction

The presence of atrial fibrillation (AF) impairs quality of life[1] and worsens long-term prognosis.[2] The natural history of AF is characterized by a gradual shift from rare and short-lasting episodes (paroxysmal AF) to progressively more frequent and persisting relapses (persistent/permanent AF).[3] Several factors, including presence of comorbidities,[4] underlying cardiomyopathies,[5] clinical subtype,[6–8] and duration[9] of the arrhythmia in patients treated with pharmacologic therapy, have been related to an increased risk for AF progression over time. In addition, patient's and physician's belief[10,11] plays a major role in modulating AF progression and represents an area in which the greatest efforts should be invested. Although transcatheter ablation, a valuable and increasingly proposed option for treatment of symptomatic drug-resistant AF,[12] holds the potential to interfere and delay this process, few data are available on progression to permanent AF following AF transcatheter ablation (AFTCA).

The main aim of the present study is to report on the long-term progression rate to permanent AF in a large cohort of patients undergoing AFTCA in a single high-volume center.

Methods

Consecutive patients referred to our center between 2004 and 2010 for AFTCA were included in this retrospective study.

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Clinical features of the study population, procedural and periprocedural details, and follow-up data were routinely recorded. AF progression was defined as the shift from paroxysmal or persistent/long-standing persistent AF to permanent AF. Permanent AF, according to latest European Society of Cardiology guidelines,[13] was defined when the presence of the arrhythmia was accepted by the patient and the physician, leading to a rate control strategy.

Ablation procedure

Procedural details have been reported elsewhere.[14] In brief, the ablation approach encompassed antral pulmonary vein isolation (PVI) in all cases of paroxysmal lone AF (i.e., AF in the absence of any clinical, ECG, or structural abnormality). Antral PVI with the addition of linear lesions and complex fractionated atrial electrogram ablation was performed in patients with persistent/long-standing persistent AF and/or confirmed structural heart disease (e.g., congenital, hypertrophic, dilated cardiomyopathy, coronary artery disease, or valvular heart disease). In case of redo procedure due to paroxysmal lone AF and documented pulmonary vein reconnection, antral PVI alone was newly performed.

Follow-up

Recurrences were detected by routine ambulatory visits (performed at 1, 3, and 6 months and yearly thereafter), with collection of patients' symptoms and 24-hour Holter ECG recordings. Rhythm or rate control strategy was registered according to the referring physician's advice as to the type of antiarrhythmic drugs prescribed.

Statistical analysis

Categorical variables are reported as count and percentage. Continuous variables are reported as median and interquartile range (IQR). Correlations between baseline characteristics and AF progression were tested in cross tabulation tables by Pearson χ^2 or Fisher exact test and by 1-way analysis of variance for categorical and continuous variables, respectively. To test the independent correlation of these parameters with AF progression, all variables reporting a significant correlation at univariate analysis were included in a stepwise multivariate logistic regression model. Kaplan-Meier curves were used to measure AF progression-free survival over time stratified for lone AF or not and compared by log-rank test. Two-sided $P < .05$ was considered significant. All analyses were performed with SPSS 16.0 (SPSS Inc, Chicago, IL).

Results

Eight hundred eighty-nine patients (mean age 57 ± 11 years, 78% male) underwent AF ablation between January 2001 and September 2010. Baseline features of the study population are listed in Table 1. Paroxysmal AF was detected in 474 patients (53.3%), persistent AF in 360 (40.5%), and long-standing AF in 55 (6.2%). In order to achieve stable long-term rhythm control, 276 patients (31%) underwent redo procedures (Figure 1). The first redo procedure was performed a median of 11.2 months (IQR 6.2–22.4 months) after the first transcatheter ablation.

Ablation protocol according to baseline AF classification is detailed in Table 2. The overall cumulative AF progression

Table 1 Baseline, procedural, and echocardiographic features of the study population stratified by arrhythmia progression over long-term follow-up

	Total (n = 889)	AF progression (n = 57)	No AF progression (n = 832)	*P* value
Male sex	696 (78.3)	36 (63.2)	660 (79.3)	
Age ≥65 years	244 (27.4)	23 (40.4)	221 (26.6)	.023
Hypertension	410 (46.1)	30 (52.6)	380 (45.7)	.338
Body mass index	27 ± 7	27 ± 4	27 ± 6	.810
Diabetes mellitus	32 (3.6)	3 (5.3)	29 (3.5)	.453
Heart failure	43 (4.8)	6 (10.5)	37 (4.4)	.051
Previous hyperthyroidism	94 (10.6)	13 (22.8)	81 (9.7)	.006
Previous hypothyroidism	72 (8.1)	5 (8.8)	67 (8.1)	.802
Cerebral stroke/transient ischemic attack	84 (9.4)	7 (12.3)	77 (9.3)	.479
$CHADS_2$ score ≥2	143 (16.1)	15 (26.3)	128 (15.4)	.039
CHA_2DS_2Vasc ≥2	335 (37.7)	32 (56.1)	303 (36.4)	.004
Structural cardiomyopathy	197 (22.2)	30 (52.6)	167 (20.1)	<.001
Lone AF	266 (29.9)	0 (0.0)	266 (32.0)	<.001
Paroxysmal AF	474 (53.3)	13 (22.8)	461 (55.4)	<.001
Persistent AF	360 (40.5)	36 (63.2)	324 (38.9)	
Long-standing persistent AF	55 (6.2)	8 (14.0)	47 (5.6)	
Ablation protocol				
PVI	198 (22.3)	7 (12.3)	191 (23.0)	.141
PVI + linear lesions	500 (56.2)	38 (66.6)	462 (55.5)	
PVI + linear lesions + CFAE	191 (21.5)	12 (21.1)	179 (21.5)	
Echocardiography				
Left atrial anteroposterior diameter (mm)	46 ± 7	50 ± 7	46 ± 6	<.001
Left atrial superoinferior diameter (mm)	61 ± 8	68 ± 7	61 ± 8	<.001

Values are given as no. (%) or mean ± SD.

AF = atrial fibrillation; CFAE = complex fractionated atrial electrogram; PVI = pulmonary vein isolation.