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Ablation strategies for different types of atrial fibrillation in Europe: results of the ESC-EORP EHRA Atrial Fibrillation Ablation Long-Term registry

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Aims	The ESC EORP EHRA Atrial Fibrillation (AF) Ablation Long-Term registry was designed to assess management and outcomes of AF catheter ablation procedures in Europe. To investigate the current ablation approaches and their outcomes for patients with paroxymal AF (PAF) and non-PAF in Europe.
Methods and results	Data from index ablations were collected in 27 European countries at 104 centres in a prospective fashion. Pre-procedural, procedural, and 1-year follow-up data were captured on a web-based electronic case record form. Data on the ablation procedure were available for 3446 patients. Of these, 2513 patients and 933 patients underwent pulmonary vein isolation (PVI) or PVI plus (PVIplus) additional ablation, respectively. The ablation strategy was limited to PVI in 81% and 56% of patients in the PAF and non-PAF group, respectively ($P < 0.001$). In the non-PAF group, left atrial linear ablation and ablation of complex fragmented atrial electrograms were more commonly performed. Arrhythmias recurrence after PVI was 29% and 39% in the PAF and non-PAF group, respectively ($P < 0.001$) and 42% after PVIplus in both groups. Atrial fibrillation related hospital admissions were more common in the PVIplus group (20% vs. 14%). A very low procedural complication rate was observed. No relevant differences were observed with regard to repeat ablation (PVI 9% and PVIplus 11%).
Conclusion	In patients with PAF and non-PAF, the ablation strategies of PVI and PVIplus led to similar arrhythmia-free survival rates after 1 year. A considerable hospital readmission rate was noted.
Keywords	Atrial fibrillation • Ablation • Strategies • Registry • EHRA

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What's new?

- The present analysis provides unique insight into contemporary ablation strategies for patients with paroxymal atrial fibrillation (PAF) and non-PAF in Europe.
- Pulmonary vein isolation remains the predominant ablation strategy for PAF and non-PAF.
- The incidence of serious procedure-related complications was low.
- Adding ablation lesions to PVI did not result in improved outcomes.
- In the first year after atrial fibrillation ablation, a considerable number of patients were re-admitted, required repeat ablation and were taking antiarrhythmic drug therapy.

Introduction

Catheter ablation has become an important treatment modality for patients with symptomatic drug-refractory paroxysmal and non-paroxysmal atrial fibrillation (PAF/non-PAF).¹ Pulmonary vein isolation (PVI) remains the cornerstone of any ablation procedure irrespective of patient characteristics.² Beyond PVI, various ablation strategies have been proposed and have been implemented into clinical practice although scientific evidence from randomized studies was scarce. Amongst others, strategies include ablation of complex fractionated atrial electrograms (CFAE),³ linear lesions, ablation of lowvoltage areas (i.e. substrate modification),⁴ as well as identification and ablation of rotational activities and putative atrial fibrillation (AF) trigger sites.⁵ Most recently, current approaches have been called into question by the results of the STAR AF 2 trial failing to demonstrate any benefit of complex left atrial (LA) ablation after PVI had been achieved.⁶ The European Society of Cardiology (ESC) sponsored EURObservational Research Programme on AF Ablation Long-Term (EORP-AFA LT) registry aimed to assess management and outcomes of AF catheter ablation procedures in Europe.⁷ The present analysis was designed to investigate current ablation approaches and their outcomes for patients with PAF and non-PAF in Europe.

Methods

Study design

The EORP AF Long-Term Ablation registry was set-up by EORP at the ESC to collect data on ablation procedures across Europe. Data from index ablations were collected in 27 European countries at 104 centres in a prospective fashion.

The details of this registry had been described in detail elsewhere.⁷ In brief, National Societies of Cardiology were invited to participate in the registry by assisting in the inclusion of centres and updating the investigators and the ESC with the legal and ethical requirements. All centres performing AF ablation in each country were invited, independent of the number of annual procedures. National coordinators obtained approval by the national and/or local Institutional Review Board, depending on regulations in each country.

Between April 2012 and April 2015, centres were asked to enroll all consecutive patients up to a maximum of 50 patients per centre.

Data collection

Data were captured on a web-based electronic case record form. Data collection included demographic variables, procedural, and post-procedural data as well as the 12 months of follow-up status. The latter was performed according to the centres' standard. On-site monitoring was performed in 23/104 hospitals.

Statistical analysis

Statistical analysis was performed using SAS statistical software version 9.4 (SAS Institute, Inc., Cary, NC, USA). Categorical variables were expressed using counts and percentages. Frequencies were compared using the Fisher's exact test. *P*-values less than 0.05 are considered statistically significant.

Results

Study population

In total, 3660 patients were enrolled into the registry. Due to missing data (n = 30) or because ablation had not been performed (n = 37), 3593 patients (2428 PAF and 1165 non-PAF) were analysed and 3180 (89%) completed the 1-year follow-up.

Details of demographic variables are given in *Table 1*. Two-thirds of the patient population were male and the mean age was 58 ± 10 years. Patients were mildly obese (mean body mass index 28 ± 5) and presented with few comorbidities as reflected by the relatively low median CHA₂DS₂-VASc score of 1 (interquartile range q1–q3: 1–2). Patients in the non-PAF group more frequently presented with a history of hypertension and a higher number of previous electrical cardioversion. Pre-procedural echocardiography revealed a larger LA diameter in the non-PAF group.

Before ablation, 90% of patients had tried at least one antiarrhythmic drug (AAD). While the use of Class I AADs was more common in the PAF population, Class III AAD drugs were more commonly used in the non-PAF group.

Ablation strategy

Data on the ablation procedure were available for 3446 patients. Of these, 2513 patients and 933 patients underwent PVI or PVIplus additional ablation, respectively.

Pulmonary vein isolation only ablation

The ablation strategy was limited to PVI only in 1894 (81%) of PAF patients and in 619 (56%) of non-PAF patients (*Table 2*). Patients who were assigned to PVI had a smaller LA diameter $(42 \pm 6 \text{ mm vs.} 44 \pm 7 \text{ mm})$ than patients undergoing additional ablation.

The most frequently used energy source for ablation was radiofrequency current (78% of all ablations). As expected, open or closed irrigated radiofrequency current ablation was dominant (75%), but non-irrigated ablation (1%) and duty-cycled ablation (2%) were also used in few cases. Among balloon catheters cryoballoon ablation was used in 21% of cases, in particular for patients with PAF (23% vs. 15% of all non-PAF patients; P < 0.001). Other balloon technologies were rarely used [laser balloon; n = 25 (1%) and high intensity focused ultrasound; n = 2 (0.1%)].

The procedural endpoint of entrance block to the pulmonary vein (PV) was achieved in the vast majority of cases but slightly differed for

Table I Demographic data

Variables	Modality	Total (N = 3593)	Non paroxysmal AF (N=1165)	Paroxysmal AF (N = 2428)	P-value
Age (years)	N	3592	1164	2428	<0.001
	Mean (SD)	57.9 (10.3)	58.9 (9.9)	57.4 (10.5)	
Gender	Female	1146/3593 (31.9%)	300/1165 (25.8%)	846/2428 (34.8%)	<0.001
Chronic heart failure		537/2418 (22.2%)	235/869 (27.0%)	302/1549 (19.5%)	<0.001
NYHA class	NYHAI	172/537 (32.0%)	74/235 (31.5%)	98/302 (32.5%)	0.501
	NYHA II	306/537 (57.0%)	130/235 (55.3%)	176/302 (58.3%)	
	NYHA III	56/537 (10.4%)	29/235 (12.3%)	27/302 (8.9%)	
	NYHA IV	3/537 (0.6%)	2/235 (0.9%)	1/302 (0.3%)	
Hypertension		1954/3579 (54.6%)	686/1162 (59.0%)	1268/2417 (52.5%)	< 0.001
Diabetes mellitus		347/3583 (9.7%)	128/1161 (11.0%)	219/2422 (9.0%)	0.060
Chronic kidney disease		57/3556 (1.6%)	26/1141 (2.3%)	31/2415 (1.3%)	0.027
Previous stroke		117/230 (50.9%)	42/82 (51.2%)	75/148 (50.7%)	0.937
Previous transient ischaemic attack		95/227 (41.9%)	28/82 (34.1%)	67/145 (46.2%)	0.077
Coronary artery disease		449/2380 (18.9%)	152/854 (17.8%)	297/1526 (19.5%)	0.320
CHADS ₂ -VASC score	Median (Q1–Q3)	1.0 (1.0–2.0)	2.0 (1.0–3.0)	1.0 (1.0–2.0)	0.002
Previous electrical cardioversion		1476/3512 (42.0%)	812/1146 (70.9%)	664/2366 (28.1%)	<0.001
LVEF (%)	Mean (SD)	59.7 (8.4)	57.2 (9.5)	60.9 (7.6)	<0.001
Left atrial diameter	Mean (SD)	42.6 (6.6)	44.7 (6.7)	41.5 (6.3)	< 0.001
Previous antiarrhythmic drug (AAD) trial		3202/3558 (90.0%)	1015/1150 (88.3%)	2187/2408 (90.8%)	0.017
AAD class					
Class I (Flec/Diso/Propa/Quinidine)		2078/3185 (65.2%)	531/1005 (52.8%)	1547/2180 (71.0%)	<0.001
Class III (Amiodarone/Sotalol)		2114/3188 (66.3%)	741/1009 (73.4%)	1373/2179 (63.0%)	<0.001

AF, atrial fibrillation; EHRA, European Heart Rhythm Association; LVEF, left ventricular ejection fraction; NYHA, New York Heart Failure Association; SD, standard deviation.

each PV: left superior PV (LSPV) 98%, left inferior PV 98%, right superior PV 97%, and right inferior PV 96%.

The average procedure time (catheter insertion to removal) was 162 ± 63 min without any difference between PAF and non-PAF patients. Mean fluoroscopy duration was 25 ± 22 min.

One fatal event was observed in 2512 procedures (0.04%). The event was considered procedure related because the patient took a fatal course after developing atrio-to-oesophageal fistula. Another two patients experienced cardiac arrest before discharge. The rate of cardiac perforation during PVI was 1.4% (1.6% vs. 0.5% for PAF and non-PAF; P = 0.03). No statistical significant difference was found between cryoballoon ablation (7/570; 1.2%) and radiofrequency ablation (39/2828; 1.4%; P = 1.0).

Thromboembolic events were observed in nine patients (0.3%) including three strokes and six patients with transient ischaemic attack. Phrenic nerve palsy was reported in 14 patients (0.6%), of which 13 occurred in the PAF and 1 in the non-PAF group. In 22 patients (0.9%), 23 vascular access complications were observed including hemo-/pneumothorax (n = 2), arteriovenous fistula (n = 8), and pseudoaneurysm (n = 13).

Pulmonary vein isolation plus ablation

Pulmonary vein isolation rates ranged from 93% (LSPV) to 94% (all other PVs) in this subgroup (*Table 3*). Additional ablation beyond PVI was performed in 933 patients (27%). While in the PAF population only 19% additional ablation lesions were performed, in the non-PAF

population 44% of patients received additional ablation. This included linear ablation in the left atrium in 32% of patients, of which 51% received a roof line and 26% a LA isthmus line. Bidirectional conduction block across the lines was achieved in 80% and 82% for the roof and the LA isthmus, respectively.

Other strategies included ablation of CFAE (33%), ablation of ganglionated plexi (35%), and isolation of the superior vena cava (4%).

In the non-PAF group, LA linear ablation and ablation of CFAE were more commonly performed (roof line 27% vs. 8%; LA isthmus line 13% vs. 4%; CFAE ablation 15% vs. 6%, ganglionated plexi ablation 11% vs. 9%; P < 0.001 for all).

Mean procedure duration was 175 ± 72 min including a fluoroscopy time of 25 ± 20 min.

No peri-procedural death was observed. The rate of cardiac perforation for PVIplus was 1.0% (1.1% vs. 0.8% for PAF and non-PAF; P = 0.75). One patient experienced cardiac arrest before discharge. In two patients (0.2%), a transient ischaemic attack was noted. Phrenic nerve palsy was reported in one patient (0.1%) in the PAF group (e.g. 2.5% of all cryoballoon ablations). In 10 patients, 12 vascular access complications were observed (1.1%) including pneumothorax (n = 1), arterio-venous fistula (n = 8), and pseudoaneurysm (n = 3).

Follow-up

The median follow-up after the index procedure was 12 months (q1–q3: 12–13 months). During follow-up, 9 (0.4%) and 5 (0.6%) died in the PVI and PVI plus group, respectively (*Tables 4* and 5).

Table 2 Procedural data for PVI

Variables	Modality	Total (<i>N</i> = 2513)	Non paroxysmal AF (N = 619)	Paroxysmal AF (N = 1894)	P-value
Age (years)	Mean (SD)	57.8 (10.4)	58.9 (9.7)	57.4 (10.6)	0.002
Gender	Female	789/2513 (31.4%)	149/619 (24.1%)	640/1894 (33.8%)	<0.001
Left atrial diameter (mm)	Mean (SD)	41.8 (6.2)	43.9 (6.1)	41.1 (6.0)	<0.001
LVEF (%)	Mean (SD)	59.8 (8.1)	57.1 (9.2)	60.7 (7.5)	<0.001
Ablation modality					
Non-irrigated radiofrequency		26/2513 (1.0%)	3/619 (0.5%)	23/1894 (1.2%)	0.119
Radiofrequency with closed irrigation		100/2513 (4.0%)	32/619 (5.2%)	68/1894 (3.6%)	0.081
Radiofrequency with opened irrigation		1779/2513 (70.8%)	474/619 (76.6%)	1305/1894 (68.9%)	<0.001
Duty-cycled radiofrequency energy		50/2513 (2.0%)	4/619 (0.6%)	46/1894 (2.4%)	0.006
Сгуо		530/2513 (21.1%)	92/619 (14.9%)	438/1894 (23.1%)	<0.001
Laser balloon (endoscopic ablation system)		25/2513 (1.0%)	9/619 (1.5%)	16/1894 (0.8%)	0.185
High intensity focused ultrasound		2/2513 (0.1%)	0/619 (0.0%)	2/1894 (0.1%)	1.000
Complications					
In-hospital death (discharge)		1/2512 (0.0%)	0/618 (0.0%)	1/1894 (0.1%)	1.000
Cardiac arrest		2/2509 (0.1%)	1/618 (0.2%)	1/1891 (0.1%)	0.432
Pericardia effusion/tamponade		34/2509 (1.6%)	3/618 (0.5%)	31/1891 (1.6%)	0.031
Phrenic nerve damage		14/2510 (0.6%)	1/618 (0.2%)	13/1892 (0.7%)	0.210
Stroke		3/2511 (0.1%)	0/618 (0.0%)	3/1893 (0.2%)	1.000
TIA		6/2510 (0.2%)	1/618 (0.2%)	5/1892 (0.3%)	1.000
A-V fistula		8/2509 (0.3%)	2/617 (0.3%)	6/1892 (0.3%)	1.000
Bleeding requiring transfusion		2/2507 (0.1%)	1/617 (0.2%)	1/1890 (0.1%)	0.432
Haematoma requiring evacuation or transfusion		8/2508 (0.3%)	2/617 (0.3%)	6/1891 (0.3%)	1.000
Pseudoaneurysm		13/2507 (0.5%)	3/617 (0.5%)	10/1890 (0.5%)	1.000
Procedure duration (min)	Mean (SD)	162.1 (63.0)	157.6 (58.8)	163.6 (64.3)	0.119
Fluoroscopy time (min)	Mean (SD)	25.0 (21.6)	22.0 (18.8)	26.0 (22.4)	<0.001

AF, atrial fibrillation; LVEF, left ventricular ejection fraction; SD, standard deviation; TIA, transient ischaemic attack.

After PVI only, 31% of all patients experienced a documented arrhythmia recurrence, including 29% and 39% of patients in the PAF and non-PAF group, respectively (P < 0.001; *Figure 1*). After PVIplus, 42% of patients had a documented arrhythmia recurrence in both groups (P = 0.7).

The majority of arrhythmia recurrences were AF (85%) and fewer atrial tachycardias (15%).

The arrhythmia recurrence rates post-blanking were 23.8% in the PVI group (PAF 22.6% vs. non-PAF 27.6%; P = 0.018) and 32% in the PVIplus group (PAF 32.7% vs. non-PAF 31.3%; P = 0.675).

Arrhythmia related hospital admissions after ablation occurred in 14% and 20% in the PVI and PVIplus group, respectively (P < 0.001). For both groups, no differences between PAF and non-PAF were observed.

During follow-up, 178 and 91 patients underwent electrical cardioversion in the PVI and PVIplus group, respectively. This relates to 114 and 155 cardioversions in the PAF and non-PAF group, respectively.

After PVI, 9% of patients received a repeat ablation. A single intervention was carried out in 190 patients, two and three ablation procedures in 11 and 1 patient, respectively. Of these, 9 (4%) and 6 (3%) patients underwent surgical ablation and atrioventricular (AV) node ablation, respectively. After PVIplus 11% of patients were re-ablated during 1, 2, or 3 procedures in 74, 8, and 2 patients. This included surgical ablation and AV node ablation, in 4 (5%) and 2 (2%) patients, respectively. For both ablation strategies, no relevant differences were observed between patients with PAF and non-PAF. Notably, atypical atrial flutter ablation was more commonly performed after an index PVIplus procedure compared to PVI (24% vs. 9%; P < 0.0001).

Overall, the use of membrane active AAD significantly decreased from 56% of patients at baseline to 32% of patients at 12 months of follow-up after PVI (P < 0.001). However, 15% of patients still used a Class I AAD (no difference between PAF and non-PAF) and 16% of patients used Class III AAD (15% in PAF and 20% in non-PAF; P = 0.003).

Similarly, in the PVIplus group, the proportion of patients on-AAD decreased from 63% to 34% at 12 months of follow-up (P < 0.0001). In detail, Class I AAD were more often used in the PAF group (18% vs. 11%; P < 0.003), but Class III AAD were more often used in the non-PAF group (30% vs. 21%; P = 0.007).

Thromboembolic complications occurred in 7 (0.3%) and 1 patient (0.1%) in the PVI and PVIplus group, respectively. In 12 (0.5%) and 11 (1.4%) patients, a pacemaker was implanted.

Table 3 Procedural Data for PVI+

Variables	Modality	Total (N = 933)	Non paroxysmal AF (N = 478)	Paroxysmal AF (N = 455)	P-value
Age (years)	Mean (SD)	58.1 (9.9)	58.7 (9.9)	57.4 (9.8)	0.153
Gender	Female	310/933 (33.2%)	135/478 (28.2%)	175/455 (38.5%)	<0.001
Left atrial diameter (mm)	Mean (SD)	44.4 (7.4)	45.8 (7.3)	43.1 (7.2)	<0.001
LVEF (%)	Mean (SD)	59.6 (9.1)	57.4 (10.0)	61.6 (7.7)	<0.001
Ablation modality					
Non-irrigated radiofrequency		17/933 (1.8%)	8/478 (1.7%)	9/455 (2.0%)	0.728
Radiofrequency with closed irrigation		26/933 (2.8%)	12/478 (2.5%)	14/455 (3.1%)	0.599
Radiofrequency with opened irrigation		868/933 (93.0%)	449/478 (93.9%)	419/455 (92.1%)	0.268
Duty-cycled radiofrequency energy		5/933 (0.5%)	2/478 (0.4%)	3/455 (0.7%)	0.679
Cryo		17/933 (1.8%)	3/478 (0.6%)	14/455 (3.1%)	0.005
High intensity focused ultrasound		6/933 (0.6%)	5/478 (1.0%)	1/455 (0.2%)	0.218
Ablation of autonomic ganglionated plexi		323/932 (34.7%)	122/477 (25.6%)	201/455 (44.2%)	<0.001
Left atrial linear lesion		301/932 (32.3%)	164/477 (34.4%)	137/455 (30.1%)	0.163
Roof line		479/933 (51.3%)	296/478 (61.9%)	183/455 (40.2%)	<0.001
Mitral isthmus line		239/933 (25.6%)	143/478 (29.9%)	96/455 (21.1%)	0.002
Other left atrial linear lesion		110/933 (11.8%)	74/478 (15.5%)	36/455 (7.9%)	<0.001
Ablation at fractionated electrogram sites in		305/932 (32.7%)	166/477 (34.8%)	139/455 (30.5%)	0.167
the left and/or right atrium					
Superior vena cava		33/933 (3.5%)	17/478 (3.6%)	16/455 (3.5%)	0.974
Complications					
In-hospital death (discharge)		0	0	0	NA
Cardiac arrest		1/928 (0.1%)	1/475 (0.2%)	0/453 (0.0%)	1.000
Phrenic nerve damage		1/933 (0.1%)	0/478 (0.0%)	1/455 (0.2%)	0.488
Pericardial effusion/tamponade		9/928 (1.1%)	4/475 (0.8%)	5/453 (1.1%)	0.75
Stroke		0	0	0	NA
TIA		2/933 (0.2%)	1/478 (0.2%)	1/455 (0.2%)	1.000
A-V fistula		8/933 (0.9%)	4/478 (0.8%)	4/455 (0.9%)	1.000
Bleeding requiring transfusion		2/933 (0.2%)	1/478 (0.2%)	1/455 (0.2%)	1.000
Haematoma requiring evacuation or transfusion		3/933 (0.3%)	2/478 (0.4%)	1/455 (0.2%)	1.000
Pseudoaneurysm		3/933 (0.3%)	2/478 (0.4%)	1/455 (0.2%)	1.000
Procedure duration (min)	Mean (SD)	174.7 (72.2)	182.8 (71.2)	166.4 (72.3)	<0.001
Fluoroscopy time (min)	Mean (SD)	24.5 (20.3)	24.3 (21.6)	24.6 (18.7)	0.115

AF, atrial fibrillation; LVEF, left ventricular ejection fraction; NA, not applicable; SD, standard deviation; TIA, transient ischaemic attack.

Discussion

The present analysis provides unique insight into contemporary ablation strategies for patients with PAF and non-PAF in Europe. Data show that PVI remains the cornerstone of any AF ablation procedure both for PAF and non-PAF patients who have previously failed AAD treatment. This underlines the general adherence with expert consensus recommendations.

Safety of atrial fibrillation catheter ablation

Safety is of utmost importance when treating a non-lethal arrhythmia. The procedural serious adverse event rate in this registry was very low including a procedure-related mortality of 0.03% regardless of the ablation approach. This is a relevant decrease in comparison to

previously published data, reporting a mortality rate of 0.15%.⁸ Recently, unequivocal evidence was provided that in-hospital mortality after AF catheter ablation declined with centre's case volume.⁹ This underscores the need for transparent quality reporting and subsequently definition of parameters to qualify as an ablation centre.

Similarly, the rate of thromboembolic complications was low compared to historic data at 0.3%. One key factor of achieving such a low thromboembolic complication rate is to perform the ablation procedure with uninterrupted anticoagulation.¹⁰ Notably, more extensive ablation beyond PVI did not increase the risk for peri-procedural complications.

Selecting ablation strategies

Traditionally, type of AF (PAF vs. non-PAF) was the first parameter to decide on an individual ablation strategy (PVI vs. PVIplus).

Table 4 Follow-up data for PVI

Variables	Modality	Total (N = 2513)	Non paroxysmal AF (N = 619)	Paroxysmal AF (N = 1894)	P-value
FU time (in months)	Mean (SD)	12.8 (3.4)	12.7 (2.9)	12.8 (3.5)	0.240
Death during 12-month FU		9/2300 (0.4%)	5/560 (0.9%)	4/1740 (0.2%)	0.044
Hospitalizations due to AF, atrial flutter, or atrial tachycardia		313/2271 (13.8%)	88/554 (15.9%)	225/1717 (13.1%)	0.099
Stroke		2/2314 (0.1%)	0/567 (0.0%)	2/1747 (0.1%)	1.000
Transient ischaemic attack		5/2314 (0.2%)	1/567 (0.2%)	4/1747 (0.2%)	1.000
Permanent pacemaker implanted		12/2301 (0.5%)	2/560 (0.4%)	10/1741 (0.6%)	0.742
Number of patients with electrical cardioversion		178	90	88	
Repeat ablation procedure					
Number of procedures	0	2048/2250 (91.0%)	486/548 (88.7%)	1562/1702 (91.8%)	0.110
	1	190/2250 (8.4%)	59/548 (10.8%)	131/1702 (7.7%)	
	2	11/2250 (0.5%)	3/548 (0.5%)	8/1702 (0.5%)	
	3	1/2250 (0.0%)	0/548 (0.0%)	1/1702 (0.1%)	
Ablation for AF		167/202 (82.7%)	51/62 (82.3%)	116/140 (82.9%)	0.917
Ablation for AT		18/202 (8.9%)	6/62 (9.7%)	12/140 (8.6%)	0.799
AVN ablation		6/202 (3.0%)	2/62 (3.2%)	4/140 (2.9%)	1.000
Arrhythmia recurrence documented		719/2296 (31.3%)	215/557 (38.6%)	504/1739 (29.0%)	<0.001
AF recurrence		619/719 (86.1%)	189/215 (87.9%)	430/504 (85.3%)	0.358
AT recurrence		98/719 (13.6%)	23/215 (10.7%)	75/504 (14.9%)	0.134
Antiarrhythmic drugs at 12-month FU					
Class I		338/2292 (14.7%)	78/555 (14.1%)	260/1737 (15.0%)	0.597
Class III		368/2292 (16.1%)	112/556 (20.1%)	256/1736 (14.7%)	0.003

AF, atrial fibrillation; AT, atrial tachycardia; AVN, atrioventricular node; FU, follow-up; SD, standard deviation.

The registry data suggest that many operators still follow this decision-making process. However, other factors such as larger LA size and the presence of comorbidities such as heart failure seem to have triggered additional LA lesion sets. Other parameters such as the presence of low-voltage areas or centre's standards were not systematically captured by the registry but may have had an influence on the applied ablation strategy.

Catheter ablation of paroxymal atrial fibrillation

Both, for patients with PAF and for patients with non-PAF PVI only was the predominantly selected ablation strategy. While irrigated radiofrequency current ablation remains the most adopted technology, the cryoballoon was used in almost every fourth patient. After the study period, the Fire and Ice trial has shown, that both technologies are equivalent in eliminating AF but the cryoballoon may be more effective in reducing repeat ablations, electrical cardioversions and in preventing re-hospitalizations.^{11,12}

Surprisingly, almost every fifth PAF patient was treated with additional ablation lesions in the left atrium. To date, no compelling evidence has been presented to support these strategies. Randomized studies and a meta-analysis have reported no additional benefit of CFAE ablation.^{13,14} In turn, ablation of ganglionated plexi in addition to PVI is supported by the results of a randomized pilot study,¹⁵ but since then, larger confirmatory studies have not been performed.

More recently, individualized ablation strategies tailored to the patient's LA low-voltage areas have shown to confer better outcomes.^{4,16} These results need to be confirmed in on-going multicentre randomized studies such as DECAAF II (NCT02529319).

Catheter ablation of non-paroxymal atrial fibrillation

Interestingly, a PVI strategy was used in the majority of non-PAF patients although there was widespread enthusiasm for extra PV ablation in patients with more advanced forms of AF at the time of enrolment. Nowadays, after the publication of the STAR-AF-2 study results, the strategies of adding linear lesions or the ablation of CFAE were abandoned by most centres.⁶ Despite the fact, that 56% of the non-PAF patients were treated with a PVI approach, balloon catheters were used in only 15% of cases. Today, several studies show that similar results may be achieved both with the cryoballoon as well as with the laser balloon.^{17,18}

Nonetheless, in the presence of LA low-voltage PVI strategies were found to be associated with poorer outcomes and it might be necessary to extend the ablation strategy to areas in the LA. Under these circumstances 3D mapping and tip catheter ablation remain the technology of choice.

Table 5 Follow-up data for PVI+

Variables	Modality	Total (N = 933)	Non paroxysmal AF (N = 478)	Paroxysmal AF (N = 455)	P-value
FU time (in months)	Mean (SD)	13.6 (4.1)	13.5 (4.2)	13.7 (4.1)	0.494
Death at 12-month FU		5/804 (0.6%)	2/407 (0.5%)	3/397 (0.8%)	0.683
Hospitalizations due to AF, atrial flutter, or atrial tachycardia		153/779 (19.6%)	82/394 (20.8%)	71/385 (18.4%)	0.405
Stroke		0	0	0	NA
TIA		1/810 (0.1%)	1/413 (0.2%)	0/397 (0.0%)	1.000
Permanent pacemaker implanted		11/802 (1.4%)	7/406 (1.7%)	4/396 (1.0%)	0.546
Number of patients with electrical cardioversion	Ν	91	65	26	
Repeat ablation procedure					
Number of procedures	0	711/795 (89.4%)	356/402 (88.6%)	355/393 (90.3%)	0.648
	1	74/795 (9.3%)	40/402 (10.0%)	34/393 (8.7%)	
	2	8/795 (1.0%)	4/402 (1.0%)	4/393 (1.0%)	
	3	2/795 (0.3%)	2/402 (0.5%)	0/393 (0.0%)	
Ablation for AF		59/84 (70.2%)	32/46 (69.6%)	27/38 (71.1%)	0.882
Ablation for AT		23/84 (27.4%)	13/46 (28.3%)	10/38 (26.3%)	0.842
AVN ablation		2/84 (2.4%)	1/46 (2.2%)	1/38 (2.6%)	1.000
Arrhythmia recurrence documented		339/801 (42.3%)	175/407 (43.0%)	164/394 (41.6%)	0.694
AF recurrence		281/339 (82.9%)	146/175 (83.4%)	135/164 (82.3%)	0.786
AT recurrence		66/339 (19.5%)	33/175 (18.9%)	33/164 (20.1%)	0.769
Antiarrhythmic drugs @ 12-month FU					
Class		116/797 (14.6%)	44/403 (10.9%)	72/394 (18.3%)	0.003
Class III		204/798 (25.6%)	120/404 (29.7%)	84/394 (21.3%)	0.007

AF, atrial fibrillation; AT, atrial tachycardia; AVN, atrioventricular node; FU, follow-up; NA, not applicable; SD, standard deviation; TIA, transient ischaemic attack.

One year outcome after catheter ablation

The real-world outcome data of this registry are sobering. Approximately, one-third of patients suffered from at least one symptomatic arrhythmia recurrence in the first year after ablation. More importantly, rehospitalization, repeat ablation, and the need for electrical cardioversion were considerable. Given today's economic constraints and the lack of robust data for the reduction of mortality and stroke this may have important implications for future reimbursement and more importantly for society. In the future, more data are needed on cost-effectiveness of ablation compared to medical treatment. While, for PAF patients the use of the cryoballoon appears to outperform RFC-guided ablation in this regard,¹⁹ more research is needed on the appropriate ablation strategy for non-PAF patients.

Noteworthy, the incidence of thromboembolic complications was low during the first year of follow-up although approximately 20% of patients did not receive proper oral anticoagulation therapy.

Limitation

The registry was designed to collect data on contemporary strategies for AF ablation. Despite being a prospective registry, reporting and selection bias cannot be fully excluded. All comparisons between groups have to be interpreted with caution because patient allocation was not randomized and may be subject to operator's bias. In particular, PVIplus may have been performed more frequently in patients with more extensive substrate who would have had an even poorer prognosis with a PVI approach.

Due to the non-standardized arrhythmia screening success rates may be overestimated, but the thorough follow-up on clinical endpoints provides valuable information.

Conclusion

Today, AF catheter ablation is associated with a low procedural complication rate. In patients with PAF and non-PAF, the ablation strategies of PVI and PVIplus led to similar arrhythmia-free survival rates after 1 year. Rehospitalization and repeat ablation resulted in considerable healthcare consumption in the first year of follow-up.

Supplementary material

Supplementary material is available at Europace online.

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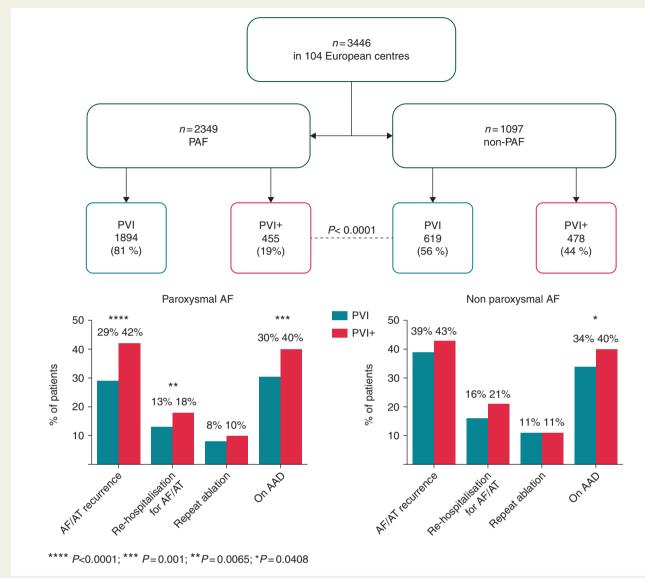


Figure 1 Outcome after AF ablation. Overview of patients with PAF and non-PAF assigned to different ablation strategies (PVI vs. PVIplus). The bar graphs illustrate 1 year outcome for several important clinical variables such as arrhythmia recurrence, rehospitalization, repeat ablation, and AAD use. The *P*-values reflect the result of χ^2 testing. AF, atrial fibrillation; AAD, antiarrhythmic drug; PAF, paroxymal AF; PVI, pulmonary vein isolation; PVIplus, PVI plus.

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References

- Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace* 2016;**18**:1609–78.
- Calkins H, Hindricks G, Cappato R, Kim Y-H, Saad EB, Aguinaga L et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: executive summary. *Europace* 2018;**20**: 157–208.

- Nademanee K, McKenzie J, Kosar E, Schwab M, Sunsaneewitayakul B, Vasavakul T et al. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. J Am Coll Cardiol 2004;43:2044–53.
- Rolf S, Kircher S, Arya A, Eitel C, Sommer P, Sergio R et al. Tailored atrial substrate modification based on low-voltage areas in catheter ablation of atrial fibrillation. Circ Arrhythm Electrophysiol 2014;7:825–33.
- Narayan SM, Krummen DE, Shivkumar K, Clopton P, Rappel W-J, Miller JM. Treatment of atrial fibrillation by the ablation of localized sources: cONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) trial. J Am Coll Cardiol 2012;60:628–36.
- Verma A, Jiang C, Betts TR, Chen J, Deisenhofer I, Mantovan R et al. Approaches to catheter ablation for persistent atrial fibrillation. N Engl J Med 2015;372: 1812–22.
- Arbelo E, Brugada J, Blomström-Lundqvist C, Laroche C, Kautzner J, Pokushalov E et al. Contemporary management of patients undergoing atrial fibrillation ablation: in-hospital and 1-year follow-up findings from the ESC-EHRA atrial fibrillation ablation long-term registry. *Eur Heart J* 2017;38: 1303–16.
- Cappato R, Calkins H, Chen S-A, Davies W, Iesaka Y, Kalman J et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol* 2010;3:32–8.
- König S, Ueberham L, Schuler E, Wiedemann M, Reithmann C, Seyfarth M et al. In-hospital mortality of patients with atrial arrhythmias: insights from the German-wide Helios hospital network of 161502 patients and 34 025 arrhythmia-related procedures. *Eur Heart J* 2018;**39**:3947–57.
- 10. Di BL, Burkhardt JD, Santangeli P, Mohanty P, Sanchez JE, Horton R et al. Periprocedural stroke and bleeding complications in patients undergoing catheter ablation of atrial fibrillation with different anticoagulation management: results from the Role of Cournadin in Preventing Thromboembolism in Atrial Fibrillation (AF) Patients Undergoing Catheter Ablation (COMPARE) randomized trial. *Circulation* 2014;**129**:2638–44.

- Kuck K-H, Brugada J, Fürnkranz A, Metzner A, Ouyang F, Chun K et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. N Engl J Med 2016;374:2235–45.
- Kuck K-H, Fürnkranz A, Chun KRJ, Metzner A, Ouyang F, Schlüter M et al. Cryoballoon or radiofrequency ablation for symptomatic paroxysmal atrial fibrillation: reintervention, rehospitalization, and quality-of-life outcomes in the FIRE AND ICE trial. Eur Heart J 2016;37:2858–65.
- Nührich JM, Steven D, Berner I, Rostock T, Hoffmann B, Servatius H et al. Impact of biatrial defragmentation in patients with paroxysmal atrial fibrillation: results from a randomized prospective study. *Hear Rhythm* 2014;11:1536–42.
- 14. Providência R, Lambiase PD, Srinivasan N, Ganesh Babu G, Bronis K, Ahsan S et al. Is there still a role for complex fractionated atrial electrogram ablation in addition to pulmonary vein isolation in patients with paroxysmal and persistent atrial fibrillation? *Circ Arrhythm Electrophysiol* 2015;8:1017–29.
- Katritsis DG, Pokushalov E, Romanov A, Giazitzoglou E, Siontis GCM, Po SS et al. Autonomic denervation added to pulmonary vein isolation for paroxysmal atrial fibrillation: a randomized clinical trial. J Am Coll Cardiol 2013;62:2318–25.
- Kircher S, Arya A, Altmann D, Rolf S, Bollmann A, Sommer P et al. Individually tailored vs. standardized substrate modification during radiofrequency catheter ablation for atrial fibrillation: a randomized study. Europace 2018;20:1766–75.
- Schmidt B, Neuzil P, Luik A, Osca Asensi J, Schrickel JW, Deneke T et al. Laser balloon or wide-area circumferential irrigated radiofrequency ablation for persistent atrial fibrillation: a multicenter prospective randomized study. *Circ Arrhythm Electrophysiol* 2017;**10**.
- Koektuerk B, Yorgun H, Hengeoez O, Turan CH, Dahmen A, Yang A et al. Cryoballoon ablation for pulmonary vein isolation in patients with persistent atrial fibrillation: one-year outcome using second generation cryoballoon. *Circ Arrhythm Electrophysiol* 2015;8:1073–9.
- Chun KRJ, Brugada J, Elvan A, Gellér L, Busch M, Barrera A et al. The impact of cryoballoon versus radiofrequency ablation for paroxysmal atrial fibrillation on healthcare utilization and costs: an economic analysis from the FIRE AND ICE trial. J Am Heart Assoc 2017;6:pii: e006043.