

# Contemporary management of patients undergoing atrial fibrillation ablation: inhospital and 1-year follow-up findings from the ESC-EHRA atrial fibrillation ablation long-term registry

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Aims	The ESC-EHRA Atrial Fibrillation Ablation Long-Term registry is a prospective, multinational study that aims at providing an accurate picture of contemporary real-world ablation for atrial fibrillation (AFib) and its outcome.
Methods and results	A total of 104 centres in 27 European countries participated and were asked to enrol 20–50 consecutive patients scheduled for first and re-do AFib ablation. Pre-procedural, procedural and 1-year follow-up data were captured on a web-based electronic case record form. Overall, 3630 patients were included, of which 3593 underwent an AFib ablation (98.9%). Median age was 59 years and 32.4% patients had lone atrial fibrillation. Pulmonary vein isolation was attempted in 98.8% of patients and achieved in 95–97%. AFib-related symptoms were present in 97%. Inhospital complications occurred in 7.8% and one patient died due to an atrioesophageal fistula. One-year follow-up was performed in 3180 (88.6%) at a median of 12.4 months (11.9–13.4) after ablation: 52.8% by clinical visit, 44.2% by telephone contact and 3.0% by contact with the general practitioner. At 12-months, the success rate with or without antiarrhythmic drugs (AADs) was 73.6%. A significant portion (46%) was still on AADs. Late complications included 14 additional deaths (4 cardiac, 4 vascular, 6 other causes) and 333 (10.7%) other complications.
Conclusion	AFib ablation in clinical practice is mostly performed in symptomatic, relatively young and otherwise healthy pa- tients. Overall success rate is satisfactory, but complication rate remains considerable and a significant portion of patients remain on AADs. Monitoring after ablation shows wide variations. Antithrombotic treatment after ablation shows insufficient guideline-adherence.
Keywords	Atrial fibrillation • Ablation • Prospective registry • Management • Outcomes • Complications

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# Introduction

Almost 20 years after its first description, catheter ablation is a widely used treatment strategy for patients with symptomatic atrial fibrillation (AFib) resistant to antiarrhythmic drugs (AADs). Unfortunately, a significant proportion of treated patients suffer from recurrences, <sup>1,2</sup> and many studies have questioned the real-world efficacy of this technique.<sup>3–5</sup> On the other hand, major and even life-threatening complications, such as cardiac perforation, stroke or atrioesophageal fistula may occur.<sup>6–8</sup> It is of utmost importance to evaluate the current real-world status of management of patients undergoing an AFib ablation, in order to evaluate trends and to identify evidence-based practice gaps that can be subject to improvement.

The Atrial Fibrillation Ablation Registry, conducted by the European Heart Rhythm Association of the European Society of Cardiology (ESC), was designed to provide an accurate picture of contemporary real-world AFib ablation and its outcome. A pilot study was conducted for validating the structure, performance, and quality of the data set.<sup>7,8</sup> We now present the results of the inhospital and 1-year follow-up analysis of the ESC-EHRA AFib Ablation Long-Term registry.

# **Methods**

# **Primary objective**

To describe the real-life clinical epidemiology of patients undergoing AFib ablation procedures, the diagnostic and therapeutic processes applied in these patients and the short- and mid-term outcomes (success and complications).

# Study design and setting

The AFib Ablation Long-term registry is a prospective, multicentre, observational registry of consecutive patients undergoing an ablation procedure for AFib at 104 centres in 27 countries within the European Society of Cardiology.

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 AFib ablation in each country were invited, independent of the number of annual AFib ablations performed, and they accepted on a voluntary basis. National Coordinators were responsible for obtaining approval by the national and/or local Institutional Review Board, depending on regulations in each country.

# Study participants

Centres were asked to enrol all consecutive patients (up to a maximum of 50) scheduled for AFib ablation procedure between April 2012 and April 2015, and to follow them up for 1 year. Both first and repeat ablations were included. There were no exclusion criteria. All patients signed an informed consent before collection of any data.

# **Data collection**

All centres were asked to complete a one-time site questionnaire describing the type and size of the centre, reference area population, facilities, and number of invasive procedures performed annually.

Data were collected using a web-based system. An electronic case report form was developed to capture the following information for each enrolled patient:

- Enrolment data: demographics, risk factors, and co-morbidities, precipitating factors, type of AFib, symptoms, pharmacological and non-pharmacological treatments, prior AFib management, invasive/ non-invasive diagnostic procedures, electrocardiographic and echocardiographic data, indications for AFib ablation.
- Procedural data: laboratory setting, catheters used, type of energy, imaging techniques, anaesthesia, anticoagulation used, ablation strategy, X-ray exposure parameters, outcome parameters used to define procedural success, and complications.
- Post-procedural data: hospital stay duration, medication after the procedure, complications.
- 12-month follow-up data: symptom status, clinical evaluations and admissions, rhythm monitoring methods, other diagnostic procedures, follow-up electrocardiographic findings, status regarding arrhythmia recurrence and type of recurrence (if any), adverse events, medication.

Centres planned their follow-up according to their usual clinical practice. The database was set up at the European Heart House of the ESC (France). The EURObservational Research Programme (EORP) Department of the ESC was responsible for close central data monitoring and auditing at each investigational site to detect inaccuracies and inconsistencies. In total 23 out of 104 (22.1%) participating centres, across 14 countries were subject to on sitemonitoring. In these centres, consecutiveness of the inclusion of patients and accuracy of the recorded data in the database compared with source data were verified.

# Definitions

Atrial fibrillation was defined as *paroxysmal*, *persistent* or *long-lasting persistent AFib* following the recommendations of the 2010 ESC Guidelines.<sup>9</sup> Lone AFib was considered in patients under 60 years of age in the absence of clinical or echocardiographic findings of other cardiovascular disease (including hypertension), pulmonary disease, and/or occult hyperthyroidism. The severity of patient-reported symptoms was classified using the EHRA Score.<sup>9</sup>

Arrhythmia recurrence was defined as an electrocardiographically documented episode of AFib or atrial flutter lasting at least 30 s. Cavotricuspid isthmus-dependent flutter was excluded from all definitions. A *blanking period* of 3 months was employed after ablation. *One-year success* was defined as patient survival free from any atrial arrhythmia, with or without AAD, as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure. Recurrences of any atrial arrhythmia within the first 3 months after the procedure were classified as *early recurrences* and were not considered as failure.

# **Statistical analysis**

All patients with unclassified type of AFib and who did not undergo ablation procedure were excluded from the analyses. The 1-year FU data of patients enrolled in the in-hospital phase was used for the analyses.

Continuous variables were reported as median and interquartile range (IQR). Group comparisons were made using a non-parametric test (Kruskal–Wallis test). Categorical variables were reported as

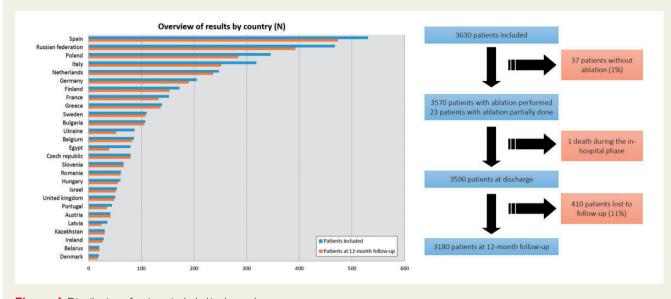


Figure I Distribution of patients included in the study.

percentages. Group comparisons were made using a chi-square test or Fisher's exact test (if any expected cell count was <5). For qualitative variables with more than two possibilities, the Monte Carlo estimates of the exact p-values are used. Plots of the Kaplan-Meier curves for arrhythmia-free survival according to type of AFib categories were performed. The survival distributions were compared using the log-rank test. A two-sided *P*-value < 0.05 was considered statistically significant.

All analyses were performed using SAS statistical software version 9.3 (SAS Institute, Inc., Cary, NC, USA). The STROBE checklist was used for appropriate reporting of the study<sup>10</sup> (*Supplementary material online, Table S1*).

# Results

# Characteristics of participating centres and patient population

Participating centres comprised 64 university hospitals, 23 community/district hospitals, and 17 private clinics, with a median number of 585.0 hospital beds (IQR 270.0–978.0). The hospital reference area included a median number of 40 000 inhabitants (IQR 18 544–160 000). The median annual number of AFib ablations in the participating centres was 113.0 (IQR 58.0–250.0), with 52 centres performing >100 ablations/year and 17 <50 ablations/year. *Figure 1* shows the flowchart of the study and the number of patients at the in-hospital and 12-follow-up by participating country.

# **Baseline clinical characteristics**

Between April 2012 and April 2015, 3630 patients were enrolled in the registry. The ablation procedure was not performed in 37 patients (1.0%): 12 patients had a left atrial (LA) thrombus, 7 patients suffered cardiac perforation during transseptal puncture (3 of them with associated tamponade), transseptal puncture was unsuccessful in 5 patients, 3 patients underwent cavotricuspid isthmus-dependent atrial flutter ablation only, 2 patients were in sinus rhythm and/or AFib could not be induced, in one repeat ablation procedure all pulmonary veins (PV) were already isolated, one patient experienced chest pain with ST-segment elevation, three individuals experienced non-procedure-related symptoms (fever, agitation, and vomiting) and in two cases technical problems occurred. These patients have only been included in the analysis of complications.

The baseline clinical characteristics of the total cohort are summarized in *Table 1*. The median age was 59.0 years (IQR 52.0–65.0). Over half of the population was hypertensive and one-third were considered obese (IMC >  $30 \text{ kg/m}^2$ ).

Two-thirds of the participants suffered from paroxysmal AFib (67.6%) with a median number of 3.0 episodes in the month previous to enrolment (IQR 1.0–8.0), while only 5% were considered to have long-lasting AFib (i.e.  $\geq$ 1 year). *Table 1* shows the clinical characteristics of AFib in the study population. A total of 1165 patients (32.4%) had lone AFib. The most common underlying disorder was hypertension with (25.7%) or without (37.3%) accompanying myocardial alterations. Prior history of atrial flutter was present in one quarter of patients (24.3%), mainly cavotricuspid isthmus-dependent (84.7%). Almost all patients (97.0%) reported AFib-related symptoms at baseline, mainly palpitations, but also fatigue, dyspnoea and weakness.

Management of AFib before opting for ablation included AAD in 90.0% of patients (median of 1.0 AAD drug trials; IQR 1.0–2.0) and electrical or pharmacological cardioversions in 66.3% of patients. The indications for AFib ablation are displayed in *Table 1*.

# Ablation procedure and in-hospital management

## **Pre-procedural evaluation**

Two-thirds of patients (67.8%) were in sinus rhythm before the procedure, with a median heart rate of 68.0 bpm (IQR 60.0–84.0 bpm). A pre-procedural transthoracic echocardiogram was done in 83.9% of individuals showing a median LA diameter of 42.0 mm (IQR 38.0– 47.0). Patients with persistent and long-standing persistent AFib had a

# Table I Baseline clinical characteristics

	All (n =3593)	Paroxysmal AFib (n =2428)	Persistent AFib (n = 985)	Long-standing persistent AFib (n = 180)
Age (years)				
n	3592	2428	985	179
Median (IQR)	59.0 (52.0–65.0)	59.0 (52.0–65.0)	60.0 (53.0–66.0)	57.0 (49.0–63.0)
Females (%)	1146/3593 (31.9%)	846/2428 (34.8%)	257/985 (26.1%)	43/180 (23.9%)
Caucasian (%)	3111/3429 (90.7%)	2136/2344 (91.1%)	843/928 (90.8%)	132/157 (84.1%)
Body mass index >30 kg/m <sup>2</sup> (%)	1047/3333 (31.4%)	659/2239 (29.4%)	327/927 (35.3%)	61/167 (36.5%)
Cardiovascular risk factors (%)				
Diabetes mellitus	347/3583 (9.7%)	219/2422 (9.0%)	104/981 (10.6%)	24/180 (13.3%)
Hypertension	1954/3579 (54.6%)	1268/2417 (52.5%)	580/983 (59.0%)	106/179 (59.2%)
Active smokers	353/3432 (10.3%)	226/2320 (9.7%)	96/936 (10.3%)	31/176 (17.6%)
Former smokers (>1 year)	653/3432 (19.0%)	426/2320 (18.4%)	200/936 (21.4%)	27/176 (15.3%)
Hypercholesterolemia	1159/3517 (33.0%)	799/2375 (33.6%)	314/966 (32.5%)	46/176 (26.1%)
lschaemic thromboembolic events (%)	230/3576 (6.4%)	148/2421 (6.1%)	73/975 (7.5%)	9/180 (5.0%)
Implanted devices				
PM	116/3590 (3.2%)	76/2425 (3.1%)	38/985 (3.9%)	2/180 (1.1%)
ICD	27/3588 (0.8%)	17/2424 (0.7%)	8/984 (0.8%)	2/180 (1.1%)
CRT-P	5/3588 (0.1%)	4/2424 (0.2%)	1/984 (0.1%)	0/180
CRT-D	7/3588 (0.2%)	4/2424 (0.2%)	3/984 (0.3%)	0/180
CHA2DS2-VASc	( )	( )	· · · ·	
0	805/3476 (23.2%)	573/2342 (24.5%)	197/964 (20.4%)	35/170 (20.6%)
1	1038/3476 (29.9%)	704/2342 (30.1%)	285/964 (29.6%)	49/170 (28.8%)
2	810/3476 (23.3%)	541/2342 (23.1%)	227/964 (23.5%)	42/170 (24.7%)
3	525/3476 (15.1%)	331/2342 (14.1%)	168/964 (17.4%)	26/170 (15.3%)
4	197/3476 (5.7%)	128/2342 (5.5%)	58/964 (6.0%)	11/170 (6.5%)
5	70/3476 (2.0%)	47/2342 (2.0%)	18/964 (1.9%)	5/170 (2.9%)
6	24/3476 (0.7%)	13/2342 (0.6%)	9/964 (0.9%)	2/170 (1.2%)
7	7/3476 (0.2%)	5/2342 (0.2%)	2/964 (0.2%)	0/170
, HAS-BLED	//3///0(0.2/0)	5/25 12 (0.270)	2/701 (0.270)	0/1/0
0	2063/3357 (61.5%)	1422/2271 (62.6%)	526/920 (57.2%)	115/166 (69.3%)
1	1009/3357 (30.1%)	682/2271 (30.0%)	287/920 (31.2%)	40/166 (24.1%)
2	241/3357 (7.2%)	139/2271 (6.1%)	93/920 (10.1%)	9/166 (5.4%)
3	39/3357 (1.2%)	23/2271 (1.0%)	14/920 (1.5%)	2/166 (1.2%)
4	5/3357 (0.1%)	5/2271 (0.2%)	0/920	0/166
<3	3313/3357 (98.7%)	2243/2271 (98.8%)	906/920 (98.5%)	164/166 (98.8%)
≥3	44/3357 (1.3%)	28/2271 (1.2%)	14/920 (1.5%)	2/166 (1.2%)
Number of AFib episodes in the last month	(0.5%)	20/22/1 (1.2/6)	14/720 (1.5%)	2/100 (1.276)
·	1978	1850	107	21
n Median (IQR)	3.0 (1.0-7.0)	3.0 (1.0-8.0)	1.0 (1.0-1.0)	1.0 (0.0-1.0)
	5.0 (1.0-7.0)	5.0 (1.0-6.0)	1.0 (1.0-1.0)	1.0 (0.0-1.0)
AFib underlying disorder (%) Lone atrial fibrillation	11( 5/2502 (22 49/)	873/2428 (36.0%)	247/00E (2E 19/)	4E/100 (DE 0%)
	1165/3593 (32.4%)	( )	247/985 (25.1%)	45/180 (25.0%)
Hypertension without known	1336/3579 (37.3%)	879/2417 (36.4%)	388/983 (39.5%)	69/179 (38.5%)
hypertensive cardiomyopathy			402/222 (24 40()	27/424 (27 (9/)
Hypertensive cardiomyopathy	623/2423 (25.7%) 299/2422 (14 F%)	394/1552 (25.4%)	192/737 (26.1%)	37/134 (27.6%)
Valvular heart disease	399/2423 (16.5%)	212/1552 (13.7%)	160/737 (21.7%)	27/134 (20.1%)
Coronary artery disease	449/2380 (18.9%)	297/1526 (19.5%)	134/724 (18.5%)	18/130 (13.8%)
Dilated cardiomyopathy	74/2426 (3.1%)	25/1556 (1.6%)	36/736 (4.9%)	13/134 (9.7%)
Hypertrophic cardiomyopathy	55/2426 (2.3%)	32/1555 (2.1%)	19/737 (2.6%)	4/134 (3.0%)
Chronic heart failure	537/2418 (22.2%)	302/1549 (19.5%)	172/736 (23.4%)	63/133 (47.4%)
Other cardiac disease	158/2415 (6.5%)	88/1548 (5.7%)	62/733 (8.5%)	8/134 (6.0%)
Hyperthyroidism	84/3519 (2.4%)	57/2385 (2.4%)	22/959 (2.3%)	5/175 (2.9%)

Continued

Table I

Symptoms

Quality of life

Desire for drug-free lifestyle

Paroxysmal AFib previously failed antiarrhythmic medication (Class IIa)

Indications according to the recommendations of the 2010 ESC AFib guidelines

Desire for sinus rhythm

Continued

Long-standing

17/178 (9.6%)

5/176 (2.8%)

23/178 (12.9%)

3/179 (1.7%)

5/172 (2.9%)

1/180 (0.6%)

2/180 (1.1%)

3/177 (1.7%)

32/168 (19.0%)

14/22 (63.6%)

7/180 (3.9%)

107/180 (59.4%)

59/180 (32.8%)

7/180 (3.9%)

173/180 (96.1%)

131/173 (75.7%)

104/173 (60.1%)

104/173 (60.1%)

94/173 (54.3%)

26/173 (15.0%)

26/173 (15.0%)

9/173 (5.2%)

131/173 (75.7%)

113/177 (63.8%)

60/165 (36.4%)

140/176 (79.5%)

26/138 (18.8%)

28/138 (20.3%)

102/139 (73.4%) 26/139 (18.7%)

1/138 (0.7%)

10/138 (7.2%)

19/138 (13.8%)

1.0 (1.0-2.0)

0/138

140

155/180 (86.1%)

128/180 (71.1%)

48/180 (26.7%)

88/180 (48.9%)

0/180

persistent AFib (n = 180)

	All (n =3593)	Paroxysmal AFib (n =2428)	Persistent AFib $(n = 985)$	Long persi (n =
AFib Precipating factors (%)				
Physical exercice	389/3502 (11.1%)	295/2366 (12.5%)	77/958 (8.0%)	17/1
Alcohol abuse	146/3481 (4.2%)	115/2358 (4.9%)	26/947 (2.7%)	5/1
Heart failure	180/3559 (5.1%)	110/2409 (4.6%)	47/972 (4.8%)	23/1
Thyreotoxicosis	57/3555 (1.6%)	37/2401 (1.5%)	17/975 (1.7%)	3/1
Sexual activity	81/3407 (2.4%)	61/2320 (2.6%)	15/915 (1.6%)	5/1
Surgical intervention	39/3560 (1.1%)	31/2406 (1.3%)	7/974 (0.7%)	1/1
Pulmonary infection	25/3561 (0.7%)	16/2407 (0.7%)	7/974 (0.7%)	2/1
Acute pericarditis	3/3564 (0.1%)	3/2409 (0.1%)	0/975	0/1
Postprandial	158/3489 (4.5%)	125/2360 (5.3%)	30/952 (3.2%)	3/1
Prior history of atrial flutter (%)	840/3461 (24.3%)	576/2343 (24.6%)	232/950 (24.4%)	32/1
Cavotricuspid-dependent flutter (%)	565/667 (84.7%)	391/448 (87.3%)	160/197 (81.2%)	14/
EHRA score for symptoms (%)				
1	107/3589 (3.0%)	68/2426 (2.8%)	32/983 (3.3%)	7/1
2	1941/3589 (54.1%)	1305/2426 (53.8%)	529/983 (53.8%)	107/1
3	1391/3589 (38.8%)	953/2426 (39.3%)	379/983 (38.6%)	59/1
4	150/3589 (4.2%)	100/2426 (4.1%)	43/983 (4.4%)	7/1
Associated symptoms (EHRA score >1)	3482/3589 (97.0%)	2358/2426 (97.2%)	951/983 (96.7%)	173/1
Palpitations	2966/3482 (85.2%)	2133/2358 (90.5%)	702/951 (73.8%)	131/1
Fatigue	1725/3482 (49.5%)	1145/2358 (48.6%)	476/951 (50.1%)	104/1
Dyspnoea	1424/3482 (40.9%)	884/2358 (37.5%)	436/951 (45.8%)	104/1
Weakness	1415/3482 (40.6%)	970/2358 (41.1%)	351/951 (36.9%)	94/1
Diziness/presyncope	621/3482 (17.8%)	449/2358 (19.0%)	146/951 (15.4%)	26/1
Chest pain	560/3482 (16.1%)	415/2358 (17.6%)	119/951 (12.5%)	26/1
Syncope	143/3482 (4.1%)	103/2358 (4.4%)	31/951 (3.3%)	9/1
Prior cardioversions (%)	2292/3457 (66.3%)	1335/2330 (57.3%)	826/954 (86.6%)	131/1
Electrical	1476/3512 (42.0%)	664/2366 (28.1%)	699/969 (72.1%)	113/1
Pharmacological	1365/3400 (40.1%)	978/2312 (42.3%)	327/923 (35.4%)	60/1
Previous AAD trial (%)	3202/3558 (90.0%)	2187/2408 (90.8%)	875/974 (89.8%)	140/1
Flecainide	1084/3178 (34.1%)	752/2175 (34.6%)	306/865 (35.4%)	26/1
Propafenone	1120/3179 (35.2%)	886/2177 (40.7%)	206/864 (23.8%)	28/1
Amiodarone	1686/3184 (53.0%)	1043/2178 (47.9%)	541/867 (62.4%)	102/1
Sotalol	923/3176 (29.1%)	682/2173 (31.4%)	215/864 (24.9%)	26/1
Quinidine	34/3172 (1.1%)	26/2172 (1.2%)	7/862 (0.8%)	1/1
Dronedarone	256/3173 (8.1%)	169/2172 (7.8%)	77/863 (8.9%)	10/1
Disopyramide	28/3172 (0.9%)	24/2172 (1.1%)	4/862 (0.5%)	0/1
Other	343/3172 (10.8%)	207/2172 (9.5%)	117/862 (13.6%)	19/1
Number of previous drug trials	. ,		. ,	
n	3202	2187	875	1
Median (IQR)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	
Reasons for AFib ablation	. ,		. ,	

All (n = 3593)

3272/3593 (91.1%)

2377/3593 (66.2%)

1068/3593 (29.7%)

1280/3593 (35.6%)

2146/3593 (59.7%)

Paroxysmal AFib

Persistent AFib

858/985 (87.1%)

600/985 (60.9%)

278/985 (28.2%)

418/985 (42.4%)

13/985 (1.3%)

2259/2428 (93.0%)

1649/2428 (67.9%)

742/2428 (30.6%)

774/2428 (31.9%)

2131/2428 (87.8%)

2/180 (1.1%)

Continued

## Table I Continued

	All (n =3593)	Paroxysmal AFib (n =2428)	Persistent AFib (n = 985)	Long-standing persistent AFib (n = 180)
Persistent symptomatic AFib refractory to antiarrhythmic therapy (Class IIa)	925/3593 (25.7%)	23/2428 (0.9%)	879/985 (89.2%)	23/180 (12.8%)
Heart failure with antiarrhythmic medication, including amiodarone, fails to control symptoms (Class IIb)	53/3593 (1.5%)	22/2428 (0.9%)	22/985 (2.2%)	9/180 (5.0%)
Prior to AAD therapy in symptomatic patients despite adequate rate control with paroxysmal AFib and no significant underlying heart disease (Class IIb)	157/3593 (4.4%)	152/2428 (6.3%)	5/985 (0.5%)	0/180
Symptomatic long-standing persistent AFib refractory to AADs (Class IIb)	147/3593 (4.1%)	2/2428 (0.1%)	13/985 (1.3%)	132/180 (73.3%)
Other	165/3593 (4.6%)	98/2428 (4.0%)	53/985 (5.4%)	14/180 (7.8%)

IQR, interquartile range; SBP, Systolic Blood Pressure; PM, pacemaker; ICD, implantable cardioverter defibrillator. CRT, cardiac resynchronization therapy. Unknown or missing values are not taken into account.

larger LA (P < 0.0001). The median left ventricular ejection fraction was 60.0% (IQR 55.0–65.0). A transesophageal echocardiogram was performed in 80.1% (within 48 h prior or during the procedure in 88.6%). The use of other tests was less frequent: holter in 32.1%, exercise in 5.9%, cardiac tomography in 41.6%, magnetic resonance in 10.3%, coronary angiography in 13.0%, and electrophysiological study in 18.8%.

#### Ablation technique

Most patients underwent a first-time AFib ablation procedure (78.4%). Repeat procedures were done either for recurrent AFib (19.1%) or LA flutter (2.6%). In 80.3% of re-do patients, just one previous procedure had been performed (median 1.0; IQR 1.0–1.0).

The procedure was done under general anaesthesia in 22.5%. Three-dimensional mapping systems were used in 79.7% of procedures, using image fusion in 35.4% (*Table 2*). The use of remote navigation and 3D rotational angiography were less frequent. The most commonly used energy source was radiofrequency with open irrigation (76.6%) followed by cryoballoon ablation (15.9%). Hybrid procedures were rare (0.2%). The median procedure duration was 160.0 min (IQR 120.0–200.0) and fluoroscopy time 19.7 min (IQR 10.7–33.1). Radiation doses are described in *Table 2*. Oesophageal monitoring was used in 8.9% mainly using a temperature probe (86.8%).

Pulmonary vein isolation was attempted in almost every patient (98.9%). In a substantial proportion of patients (21–22% of the four PV) exit block was not evaluated. Overall, PV isolation (defined as documentation of entrance and exit block when both were tested or only of entrance block when exit block was not tested) was documented in 95–97% in the four veins. Linear lesions were done in 32.7% patients, predominantly the roof in the LA (14.2%) and the right atrial (RA) cavotricuspid isthmus (18.4%). Linear ablation was more frequent in persistent and long-standing AFib. Ablation of fractionated electrograms was done in a minority (9.7%), mainly in persistent and long-standing AFib. Finally, ablation of autonomic ganglionated plexi was performed in 9.1. Detailed information on the ablation strategy per type of AFib is shown on *Table 2*.

#### Peri-procedural anticoagulation management

Before the procedure, 60.4% of patients were treated with a vitamin K antagonist and 23.0% with non-vitamin K anticoagulants (dabigatran in 14.0%, rivaroxaban in 7.6%, and apixaban in 1.4%). In one-third (30.3%), the ablation was performed on uninterrupted vitamin K antagonists with a target INR of 2.3 (IQR 2.0–2.5) and in 5.9% under uninterrupted non-vitamin K anticoagulants (dabigatran in 4.5%, rivaroxaban in 1.4%, and apixaban in 1 patient).

#### **Discharge status**

The median hospital stay was 2.0 days (IQR 1.0–4.0). At discharge, 94.9% of patients were in sinus rhythm with a median heart rate of 69.5 bpm (IQR 62.0–77.0). All patients were treated with anticoagulation therapy at discharge and 68.4% with AAD (*Figure 2*).

#### Complications related to the ablation procedure

A total of 280 patients (7.8%) experienced a procedure-related complication (Table 3). The most frequent adverse event was cardiovascular (4.1%). In particular, cardiac perforation occurred in 47 patients (1.3%). There were three non-fatal cardiac arrests (0.1%), one secondary to hypotension and ventricular fibrillation attributed to the anaesthesia, one due to sinus arrest lasting 10 min and a third of unknown origin. Cardioembolic events occurred in 11 patients (0.3%): eight transient ischemic attacks (TIAs) (0.2%) and 3 strokes (0.1%); 2 of the patients experiencing a stroke underwent the procedure using bridging from vitamin K antagonists to low molecular heparin and the third underwent the ablation under vitamin K antagonist with an INR of 3.1. In 13 out of the 15 phrenic nerve paralyses (86.7%), a cryoballoon was used. An atrio-oesophageal fistula was diagnosed by CT scan in a 49-year-old female presenting with dysphagia and cough 48 h after the procedure. The patient rapidly developed sepsis and subsequently died.

### Follow-up status

A 12-month follow-up evaluation was done at a median of 12.4 months (IQR 11.9–13.4) after the procedure by an in-person clinical

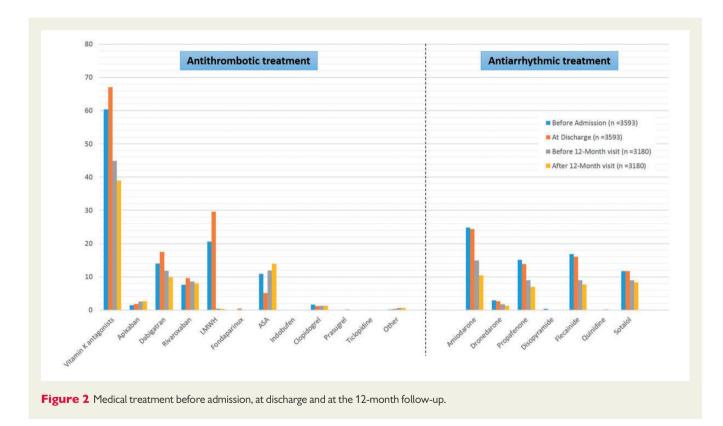
	All (n =3593)	Paroxysmal AFib (n =2428)	Persistent AFib (n = 985)	Long-standing persistent AFib (n = 180)
Type of procedure (%)				
First procedure	2815/3592 (78.4%)	1924/2428 (79.2%)	745/985 (75.6%)	146/179 (81.6%)
Redo due to Atrial Fibrillation	685/3592 (19.1%)	454/2428 (18.7%)	206/985 (20.9%)	25/179 (14.0%)
Redo due to LA Flutter/La Tachycardia	92/3592 (2.6%)	50/2428 (2.1%)	34/985 (3.5%)	8/179 (4.5%)
Hybrid AFib ablation (%)	11/3592 (0.3%)	3/2428 (0.1%)	5/985 (0.5%)	3/179 (1.7%)
Use of 3D mapping system (%)	2864/3592 (79.7%)	1838/2428 (75.7%)	863/985 (87.6%)	163/179 (91.1%)
Use of remote navigation and	190/3592 (5.3%)	117/2428 (4.8%)	58/985 (5.9%)	15/179 (8.4%)
ablation system (%)	× ,	× ,		× ,
Use of rotational angiography for	142/3592 (4.0%)	106/2428 (4.4%)	33/985 (3.4%)	3/179 (1.7%)
3D reconstruction (%)				
Use of circular mapping catheter (%)	2937/3592 (81.8%)	1962/2428 (80.8%)	838/985 (85.1%)	137/179 (76.5%)
Use of image fusion (%)	1272/3591 (35.4%)	813/2427 (33.5%)	408/985 (41.4%)	51/179 (28.5%)
CT	986/1272 (77.5%)	641/813 (78.8%)	309/408 (75.7%)	36/51 (70.6%)
MRI	180/1272 (14.2%)	102/813 (12.5%)	66/408 (16.2%)	12/51 (23.5%)
Rotational angiography	96/1272 (7.5%)	65/813 (8.0%)	29/408 (7.1%)	2/51 (3.9%)
Other	10/1272 (0.8%)	5/813 (0.6%)	4/408 (1.0%)	1/51 (2.0%)
General anaesthesia during procedure (%)	809/3592 (22.5%)	471/2428 (19.4%)	296/985 (30.1%)	42/179 (23.5%)
Energy source (%)	(,		( , , , , , , , , , , , , , , , , , , ,	
Non-irrigated radiofrequency	51/3591 (1.4%)	39/2428 (1.6%)	10/985 (1.0%)	2/178 (1.1%)
Radiofrequency with closed irrigation	126/3591 (3.5%)	82/2428 (3.4%)	39/985 (4.0%)	5/178 (2.8%)
Radiofrequency with open irrigation	2751/3591 (76.6%)	1768/2428 (72.8%)	823/985 (83.6%)	160/178 (89.9%)
Cryo	571/3591 (15.9%)	475/2428 (19.6%)	84/985 (8.5%)	12/178 (6.7%)
Duty-cycled radiofrequency energy	61/3591 (1.7%)	54/2428 (2.2%)	6/985 (0.6%)	1/178 (0.6%)
Laser balloon (endoscopic ablation system)	25/3591 (0.7%)	16/2428 (0.7%)	9/985 (0.9%)	0/178
High intensity focused ultrasound	8/3591 (0.2%)	3/2428 (0.1%)	4/985 (0.4%)	1/178 (0.6%)
Procedure duration (min)	0,007 (012,0)	0,2,20 (0,1,0)		
n	3339	2254	918	167
Median (IQR)	160.0 (120.0-200.0)	155.0 (120.0-200.0)	160.0 (120.0-200.0)	162.0 (123.0-220.0
Fluoroscopy total time (min)	100.0 (120.0 200.0)	133.0 (120.0 200.0)	100.0 (120.0 200.0)	102.0 (125.0 220.0
n	3344	2263	916	165
Median (IQR)	19.7 (10.7-33.1)	20.6 (11.3-34.0)	17.2 (9.0-32.3)	17.0 (10.7-27.1)
Radiation dose (mGy)		2010 (1110 0 110)		
n	891	617	219	55
Median (IQR)	386.0 (167.0-852.0)	379.0 (156.0-842.0)	400.0 (170.7-1000.0)	391.0 (283.0-999.0
Radiation dose (Gy/cm <sup>2</sup> )				07.110 (20010 77710
n	1872	1236	548	88
Median (IQR)	27.3 (10.0-59.5)	26.9 (9.5-57.0)	27.1 (10.1-61.9)	33.5 (16.5-102.5)
Transesophageal echocardiogram (%)	550/2783 (19.8%)	364/1845 (19.7%)	141/794 (17.8%)	45/144 (31.3%)
Intracardiac echocardiogram (%)	457/3592 (12.7%)	307/2428 (12.6%)	126/985 (12.8%)	24/179 (13.4%)
Esophageal monitoring during procedure (%)	319/3592 (8.9%)	169/2428 (7.0%)	136/985 (13.8%)	14/179 (7.8%)
Temperature probe	277/319 (86.8%)	140/169 (82.8%)	125/136 (91.9%)	12/14 (85.7%)
Electroanatomical mapping	5/319 (1.6%)	2/169 (1.2%)	2/136 (1.5%)	1/14 (7.1%)
Transeophageal echo	36/319 (11.3%)	27/169 (16.0%)	9/136 (6.6%)	0/14
Other	1/319 (0.3%)	0/169	0/136	1/14 (7.1%)
Attempt of PV isolation (overall) (%)	3509/3548 (98.9%)	2401/2414 (99.5%)	941/962 (97.8%)	167/172 (97.1%)
Achievement of PV entrance block (%)		2.0.1.2.111 (77.570)		
LSPV	3261/3374 (96.7%)	2254/2314 (97.4%)	853/898 (95.0%)	154/162 (95.1%)
LIPV	3193/3293 (97.0%)	2200/2255 (97.6%)	838/876 (95.7%)	155/162 (95.7%)
LIF V RSPV	3193/3293 (97.0%) 3236/3359 (96.3%)	2238/2303 (97.2%)	850/899 (94.5%)	148/157 (94.3%)
RIPV	. ,		( )	. ,
INIE V	3206/3352 (95.6%)	2211/2290 (96.6%)	845/902 (93.7%)	150/160 (93.8%)

# Table 2 Technical characteristics of the procedure and ablation strategy by type of atrial fibrillation

# Table 2 Continued

	All (n =3593)	Paroxysmal AFib (n =2428)	Persistent AFib (n = 985)	Long-standing persistent AFib (n = 180)
Atrial linear lesion (overall) (%)	1156/3540 (32.7%)	600/2385 (25.2%)	442/978 (45.2%)	114/177 (64.4%)
_A linear lesion (%)	606/3527 (17.2%)	231/2374 (9.7%)	293/977 (30.0%)	82/176 (46.6%)
Roof line	511/3591 (14.2%)	190/2427 (7.8%)	252/985 (25.6%)	69/179 (38.5%)
Mitral isthmus line	262/3591 (7.3%)	101/2427 (4.2%)	119/985 (12.1%)	42/179 (23.5%)
Posterior line	160/3515 (4.6%)	52/2364 (2.2%)	86/976 (8.8%)	22/175 (12.6%)
Other LA linear lesion	122/3591 (3.4%)	36/2427 (1.5%)	65/985 (6.6%)	21/179 (11.7%)
RA linear lesion (%)	716/3530 (20.3%)	433/2377 (18.2%)	22/977 (23.1%)	57/176 (32.4%)
Superior vena cava	57/3591 (1.6%)	31/2427 (1.3%)	18/985 (1.8%)	8/179 (4.5%)
Cavotricuspid isthmus ablation	660/3591 (18.4%)	406/2427 (16.7%)	204/985 (20.7%)	50/179 (27.9%)
Other RA linear lesion	29/3515 (0.8%)	10/2364 (0.4%)	15/976 (1.5%)	4/175 (2.3%)
Ablation at fractionated electrogram sites (%)	349/3590 (9.7%)	145/2427 (6.0%)	151/984 (15.3%)	53/179 (29.6%)
Ablation of autonomic ganglionated plexi	326/3590 (9.1%)	202/2427 (8.3%)	80/984 (8.1%)	44/179 (24.6%)
Jse of adenosine at end of procedure (%)	367/3591 (10.2%)	265/2427 (10.9%)	95/985 (9.6%)	7/179 (3.9%)

Unknown or missing values are not taken into account.



visit in 52.8% of cases, a telephone contact with the patient in 44.2% and a contact with the patient's general practitioner in 3.0%.

# Clinical evaluations, diagnostic procedures, and re-interventions during follow-up

Diagnostic methods for the detection of arrhythmia recurrences included periodical clinical visits with electrocardiogram in 78.4% and holter monitoring in 64.5%. Trans-telephonic monitoring and

implanted monitoring systems were seldom used (3.4% in either case). At least one electrocardiogram during follow-up was done in 86.0% of cases.

Following the ablation, 82.7% of patients had at least one cardiology evaluation and 15.8% visited the emergency room. Readmissions for AFib or flutter/tachycardia occurred in 15.4% of patients and for other cardiovascular events in 3.3%. A repeat ablation procedure was done in 9.5% of patients (median 1.0; IQR 1.0–1.0):

	At inclusion (ablation not performed) (n = 37)	In-hospital (n = 3593)	12-month FU (n = 3180)	Overall (n = 3630)
Cardiovascular (%)	7/29 (24.1%)	147/3591 (4.1%)	35/3173 (1.1%)	183/3613 (5.1%)
Pericarditis	0/29	26/3584 (0.7%)	4/3173 (0.1%)	30/3606 (0.8%)
Cardiac perforation	3/29 (10.3%)	47/3583 (1.3%)	7/3173 (0.2%)	55/3605 (1.5%)
Acute myocardial infarction	0	0	2/3173 (0.1%)	2/3605 (0.1%)
Endocarditis	0	0	2/3173 (0.1%)	2/3605 (0.1%)
Atypical atrial flutter (no AFib)	0	10/3584 (0.3%)	1/3173 (0.0%)	11/3606 (0.3%)
Bradycardia requiring pacemaker	0	5/3584 (0.1%)	5/3173 (0.2%)	10/3606 (0.3%)
Cardiac arrest	0	3/3583 (0.1%)	0/3173	3/3605 (0.1%)
Air embolism	0	8/3583 (0.2%)	1/3173 (0.0%)	9/3605 (0.2%)
Cardiac thromboembolic event	0	2/3583 (0.1%)	0/3173	2/3605 (0.1%)
Heart valve damage	0	2/3583 (0.1%)	1/3173 (0.0%)	3/3605 (0.1%)
Other	4/29 (13.8%)	55/3588 (1.5%)	15/3173 (0.5%)	73/3610 (2.0%)
Peripheral/vascular (%)	0/29	45/3591 (1.3%)	23/3173 (0.7%)	64/3613 (1.8%)
AV fistula	0	16/3589 (0.4%)	8/3080 (0.3%)	22/3518 (0.6%)
Pseudoaneurysm	0	16/3587 (0.4%)	10/3080 (0.3%)	24/3517 (0.7%)
Hematoma or bleeding requiring	0	14/3587 (0.4%)	0/3173	14/453 (3.1%)
evacuation or transfusion				
Peripheral thromboembolic event	0	0	1/3173 (0.0%)	1/3609 (0.0%)
Deep vein thrombosis	0	0	2/3173 (0.1%)	2/3609 (0.1%)
Neurological (%)	1/29 (3.4%)	26/3591 (0.7%)	10/3173 (0.3%)	36/3613 (1.0%)
Stroke	0	3/3591 (0.1%)	2/3173 (0.1%)	5/3613 (0.1%)
TIA	1/29 (3.4%)	8/3590 (0.2%)	6/3173 (0.2%)	15/3612 (0.4%)
Phrenic Nerve Damage	0	15/3590 (0.4%)	2/3080 (0.1%)	16/3520 (0.5%)
Pulmonary (%)	0/29	11/3591 (0.3%)	10/3173 (0.3%)	21/3613 (0.6%)
Hemothorax	0	1/3591 (0.0%)	0/3173	1/3613 (0.0%)
Pleural Effusion	0	5/3591 (0.1%)	0/3173	5/3613 (0.1%)
Pneumothorax	0	2/3591 (0.1%)	3/3173 (0.1%)	5/3613 (0.1%)
Pulmonary vein stenosis	0/29	3/3591 (0.1%)	4/3173 (0.1%)	7/3613 (0.2%)
Pneumonia	0	0/3591	3/3173 (0.1%)	3/3613 (0.1%)
Gastrointestinal (%)	0/29	2/3591 (0.1%)	5/3173 (0.2%)	7/3613 (0.2%)
Oesophageal ulceration	0	2/3591 (0.1%)	1/3173 (0.0%)	3/3613 (0.1%)
Esophageal fistula or perforation	0	1/3591 (0.0%)	0	1/3613 (0.0%)
Gastric motility/pyloric spam disorders	0	0/3591	3/3173 (0.1%)	3/3613 (0.1%)
General (%)	0/29	12/3591 (0.3%)	3/3173 (0.1%)	14/3612 (0.4%)
Allergic Reaction	0	9/3589 (0.3%)	2/3173 (0.1%)	11/3611 (0.3%)
Sepsis	0	1/3590 (0.0%)	0/3173	1/3612 (0.0%)
Other (%)	3/29 (10.3%)	60/3591 (1.7%)	51/3173 (1.6%)	111/3612 (3.1%)
Death (%)	0/24	1/3592 (0.0%)	14/3178 (0.4%)	15/3181 (0.5%)
Cardiac	0	0	4/14 (28.6%)	4/15 (26.7%)
Vascular	0	0	4/14 (28.6%)	4/15 (26.7%)
Non cardiovascular	0	1/1 (100.0%)	6/14 (42.9%)	7/15 (46.7%)
Overall (%)	10/23 (43.5%)	280/3591 (7.8%)	333/3098 (10.7%)	577/3538 (16.3%)

## Table 3 Adverse events associated with catheter ablation of atrial fibrillation

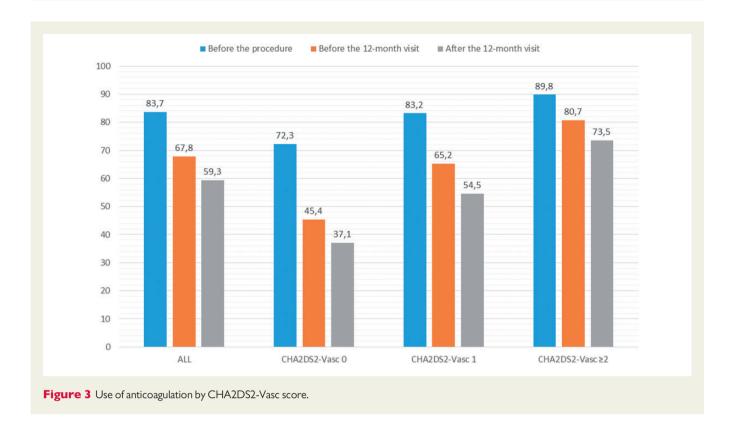
AV, atrioventricular; TIA, Transient ischemic attack.

76.3% for recurrent AFib, 15.9% for LA atrial flutter/tachycardia and 7.8% for other arrhythmias.

#### Treatment at follow-up

At the 12-month follow-up visit, 45.5% of patients were treated with AAD and two-thirds were on oral anticoagulation, both of which

were reduced following that visit (36.4 and 59.2%, respectively). After the 12-month evaluation, 37.4% of patients with CHA2DS2-Vasc 0 were still prescribed oral anticoagulation, while 26.2% of patients with CHA2DS2-Vasc  $\geq$ 2 were not (*Figure 3*). Patients with paroxysmal AFib were more likely to be off drugs compared with those with persistent or long-standing AFib (*P* = 0.0005).



#### Clinical symptoms during follow-up

Over half of the population became asymptomatic after the AFib ablation (56.6%). Palpitations, fatigue, dyspnoea and weakness were the most frequent complaints (81.5, 27.6, 20.5, and 22.4% of symptomatic patients, respectively). There was a significant improvement in the reported AFib-related symptoms after the ablation (*Figure 4*).

### Outcome of atrial fibrillation ablation

Complete data for the assessment of the 1-year outcomes of AFib ablation were available in 3065 patients (85.4%). Overall, 1086 patients (34.2%) had a documented episode of atrial arrhythmia during the 12-month follow-up period. Arrhythmia recurrence was diagnosed by a 12-lead electrocardiogram (26.7%), holter (12.7%), a hospital discharge record or written diagnosis (12.3%), an implanted monitoring system (2.0%), or trans-telephonic monitoring (1.1%). Recurrences were more frequent in persistent (39.8%) and long-standing persistent (43.7%) than in paroxysmal AFib (31.4%) (P < 0.0001). Recurrences were mainly due to AFib (29.0%), while only a minority suffered an atypical atrial flutter/tachycardia (5.5%).

During the blanking period, 656 patients (21.5%) experienced at least one episode of atrial arrhythmia (median 2.0; IQR 1.0–4.0), and 2 patients died. After the 3-month blanking window, 804 patients (26.3%) had at least 1 documented atrial arrhythmia (median 2.0; IQR 1.0–8.0); over half of them (56.5%) had had an arrhythmia recurrence also during the blanking period.

The procedure was considered successful in 2252 patients (73.6%). However, 45.0% of the total cohort was still taking AAD at the 12-month visit (33.4% of patients without documentation of arrhythmia recurrence or symptoms), although the proportion was reduced thereafter (*Figure 2*). Success rates were significantly higher

in paroxysmal AFib (*Figure 5*). Success with and without AAD is shown on *Table 4*. Despite no documentation of arrhythmias, 25.7% of patients still complained of symptoms 1 year after the ablation. On the contrary, 14.8% of patients with a documented recurrence reported being asymptomatic. As expected, persistent and, particularly, long-standing AFib, had a lower success rate.

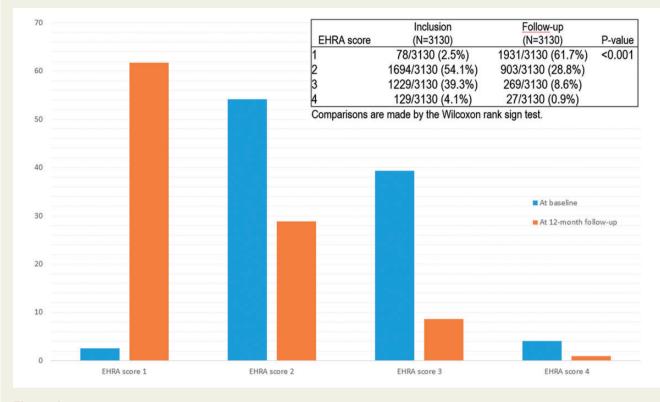
#### **Complications during follow-up**

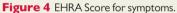
A total of 333 patients (10.7%) experienced an adverse event during follow-up. There were two strokes (one patient was under treatment with rivaroxaban and the second with clopidogrel). In addition, there were six additional TIA, two of which occurred during a repeat ablation procedure. There were also two phrenic nerve paralyses due to a repeat ablation procedure with a cryoballoon (0.1%). Other procedure-related complications included 7 cardiac perforations (0.2%) and 23 vascular complications (0.7%) (*Table 3*).

There were 14 deaths during the follow-up period. Six patients died of non-cardiovascular causes: four cancers (two lung cancers, one intestinal cancer, and one hepatocarcinoma), one infection with respiratory arrest, and one suicide. Three patients died from haemorrhagic strokes 27, 167, and 207 days after the ablation procedure, and one gastrointestinal bleeding because of colon cancer. Finally, four patients died of cardiac causes: two myocardial infarctions, one aggravated heart failure, and one cardiac arrest while sleeping (no reported autopsy).

# Discussion

Randomized clinical trials (RCTs) are considered the 'gold standard' for assessing treatment effects and are powerful designs to establish





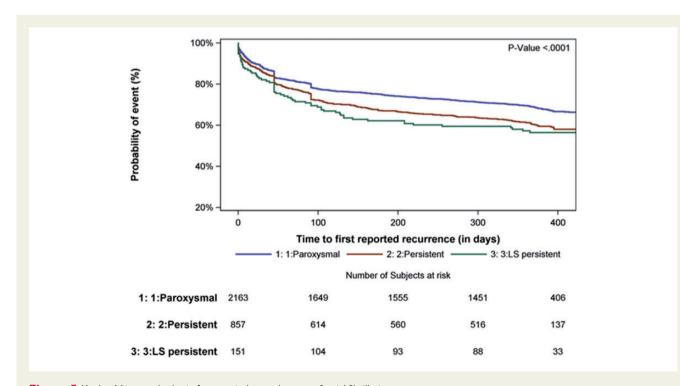


Figure 5 Kaplan-Meyer arrhythmia-free survival curve by type of atrial fibrillation.

Type AFib	No. countries	No. centres	No. patients	Success with AADs n (%) Median (IQR) between countries	Success without AADs <sup>a</sup> n (%) Median (IQR) between countries	Overall success n (%) Median (IQR) between countries
Paroxysmal	27	96	2169	956/1125 (85.0%)	563/895 (62.9%)	1566/2085 (75.1%)
				87.5 (76.9–94.4)	64.3 (56.3–77.8)	78.9 (69.0–84.3)
Persistent	27	85	859	333/423 (78.7%)	237/383 (61.9%)	587/828 (70.9%)
				80.7 (70.8–97.6)	60.4 (48.1–74.0)	70.0 (66.7–76.5)
Long-lasting persistent	18	43	152	45/67 (67.2%)	48/71 (67.6%)	99/146 (67.8%)
				73.0 (55.0–100.0)	100.0 (68.8–100.0)	75.0 (63.8–100.0)
Overall	27	96	3180	1334/1615 (82.6%)	848/1349 (62.9%)	2252/3059 (73.6%)
				85.7 (75.4–92.3)	61.4 (51.0–72.0)	76.4 (67.4–83.6)

 Table 4
 Success rates in relationship with the type of atrial fibrillation

<sup>a</sup>No discontinuation of AADs was required by the protocol.

causality. However, they provide only limited information on realworld medical practices and outcomes especially for relatively new techniques, mainly due to the selected patient sample and the strict patient monitoring. Alternatively, observational studies, if properly designed, have higher applicability in clinical practice because they include a more representative population sample and usually take place in normal healthcare settings. Several RCTs have shown better results of AFib ablation compared to AAD.<sup>1,2,11–13</sup> However, these studies had a rather small sample size of selected patient, and interventions were undertaken by experienced operators with clearly pre-specified protocols. With rising prevalence of AFib and increasingly available treatment options, it is of utmost importance to have an accurate picture of contemporary AFib ablation and its outcomes which will allow the identification of practice gaps and assist evidence-based guidelines for the management of these patients.

The ESC-EHRA Long-Term Atrial Fibrillation Ablation Registry provides a profound insight into current practice of AFib ablation across different regions of Europe, Middle East, and North Africa. When compared with the Pilot Phase,<sup>7,8</sup> the Long-Term Registry included a higher number of countries and centres and no restriction in terms of AFib procedure volumes per centre were made. With 3630 patients, it is the largest international prospective registry on indications, patient characteristics, techniques and outcomes of catheter ablation of AFib to date. Very importantly, no recommendations were provided to the participating centres in terms of medical therapy, ablation or follow-up protocol. Thus, the information retrieved provides a true snapshot of current clinical practice.

The typical patient undergoing AFib ablation is a male of 60 years with paroxysmal AFib and no evident underlying cause, very different from the profile of AFib patients in the general population.<sup>14,15</sup> On a positive note, the vast majority of patients were selected for AFib ablation following the recommendations of the current guidelines.<sup>9,16,17</sup> As expected, there was a very high proportion of symptomatic patients (97%), which is in clear discordance to the general AFib population, which is asymptomatic in 50–55%.<sup>18</sup>

A relevant finding of this registry is also the description of temporal trends in the use of technologies and management innovations. Radiofrequency energy remains the main energy source used. Surprisingly, we observed an only mild increase in the use of cryoballoon as energy source (13% in the Pilot study<sup>7</sup> vs. 16% in the current). Other energy sources such as laser, duty-cycled radiofrequency or high intensity-focused ultrasound, were only rarely used. Pulmonary vein isolation was still the most widespread ablation technique. In fact, a relatively low proportion of patients underwent further substrate modification,<sup>7</sup> in accordance to recent data that suggests no benefit in arrhythmia-free survival.<sup>19,20</sup> The inclusion of all types of centres (as opposed to only mid-to-high volume in the Pilot Registry<sup>7</sup>) did not seem to affect the procedure duration or fluoroscopy time. However, there is still clearly room for improvement as we observed a wide variation in radiation dose with some procedures close to 1 Gy of absorbed skin dose.

In peri-procedural anticoagulation, there was a shift with increasing numbers of ablations performed under uninterrupted vitamin K antagonists (19.2 in the Pilot study<sup>7</sup> vs. 30.3% now) or, in a small minority, under uninterrupted novel oral anticoagulants (0 vs. 5.9%). These regimes have been explored by several studies,<sup>21–23</sup> but until recently, there have been clear recommendations in this regard. The new 2016 ESC Guidelines on management of AFib now state that continuation of oral anticoagulation with vitamin-K antagonists (class IIb; level of evidence B) or new oral anticoagulants (class IIb; level of evidence C) should be considered during the procedure, maintaining effective anticoagulation.<sup>24</sup>

Sadly, the insufficient guideline-adherence in anticoagulation management, is still an issue in this study. Considering asymptomatic and late recurrences after AFib ablation, current guidelines<sup>9,16,17,24</sup> recommend continuation of long-term anticoagulation based on the individual thromboembolic risk independent of the assumed ablation results. Despite these recommendations, at 1 year after ablation, 26.5% of patients with CHA2DS2-VASc  $\geq$ 2 were not anticoagulated. Conversely, a third of low-risk individuals (CHA2DS2-VASc = 0) are still under oral anticoagulants. Observational findings in the general AFib population show similarly discouraging findings.<sup>14,15</sup>

Another major practice-gap that showed no significant improvement over time was the absence of appropriate assessment following the procedure. The number of clinical visits and cardiac rhythm monitoring remains suboptimal hindering the operator/centre's ability to monitor outcomes and allow comparisons. Moreover, this may contribute to inadequate anticoagulation and post-procedural AAD management. Given that only 59.5% of patients underwent serial ECG together with multiday ECG recording, the reported success rates may rather reflect percentages of patients without symptomatic recurrences. We consider this only limited post-ablation monitoring to be one of our key findings and highlights the need for more intensive monitoring in daily practice.

Naturally, the interpretation of 1-year outcomes of the procedure is limited by potential uncontrolled confounders but above all by the lack of appropriate arrhythmia monitoring. However, we can still draw several interesting conclusions. First, patient reported symptoms markedly decrease with AFib ablation and there is a significant improvement in the EHRA score. Rhythm control therapy is mainly used in symptomatic patients; however, over 50% of highly symptomatic patients do not receive adequate rate control.<sup>15</sup> Finally, the number and type of procedural complications has not changed significantly overtime, despite technological innovations and adaptations in peri-procedural management. Complication rates in this real-world population remains considerable and the risk of major (even fatal) adverse events should be taken into account. These findings reinforce the need for adherence to guidelines regarding indications and operator/centre experience.

# Limitations

This study has the inherent limitations of registries such as selection and reporting bias. To minimize these risks, we used a prospective design, requiring consecutive inclusion of patients. The EORP Department of the ESC performed extensive data validation and there was also external auditing, in order to assure quality and reliability. Eleven percent of patients were lost to follow-up, which could lead to attrition bias, but which may well reflect the clinical reality that a significant number of centres do not follow their patients. Particular effort was made by all investigators to rule out any major adverse event. The inhomogeneous and partially insufficient arrhythmia monitoring after ablation, may limit the interpretation of data on recurrences. The cross-sectional data collection complicates the identification of the exact temporal sequence of AAD management, in particular, whether it was simply continued or if it was stopped during/after the blanking period and reintroduced before the 12month visit. Being an observational study, we cannot exclude the possibility of measured or unmeasured confounding factors which may influence the study results. However, this study does not intend to establish causality but aims at being hypothesis generating and identifying practice gaps that may lead to outcomes improvement in this patient population.

# **Clinical implications**

The ESC-EHRA Long-term Atrial Fibrillation Ablation Registry provides detailed information on contemporary AFib ablation in a realworld setting. AFib ablation in clinical practice is mostly performed in symptomatic, relatively young and otherwise relatively healthy patients. Overall success rate on or off antiarrhythmics is satisfactory, but complication rate remains considerable and a significant portion of patients remain on AADs. Monitoring of patients after ablation shows wide variations. In contrast to the indications for the procedure that are consistent with current guidelines, antithrombotic treatment after ablation shows insufficient guideline-adherence.

# Supplementary material

Supplementary material is available at European Heart Journal online.

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### References

- Morillo CA, Verma A, Connolly SJ, Kuck KH, Nair GM, Champagne J, Sterns LD, Beresh H, Healey JS, Natale A, RAAFT-2 Investigators. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation (raaft-2): a randomized trial. JAMA 2014;**311**:692–700.
- Verma A, Jiang C-Y, Betts TR, Chen J, Deisenhofer I, Mantovan R, Macle L, Morillo CA, Haverkamp W, Weerasooriya R, Albenque J-P, Nardi S, Menardi E, Novak P, Sanders P. Approaches to catheter ablation for persistent atrial fibrillation. N Engl J Med 2015;**372**:1812–1822.
- Weerasooriya R, Khairy P, Litalien J, Macle L, Hocini M, Sacher F, Lellouche N, Knecht S, Wright M, Nault I, Miyazaki S, Scavee C, Clementy J, Haissaguerre M, Jais P. Catheter ablation for atrial fibrillation: are results maintained at 5 years of follow-up?. J Am Coll Cardiol 2011;57:160–166.
- 4. Scherr D, Khairy P, Miyazaki S, Aurillac-Lavignolle V, Pascale P, Wilton SB, Ramoul K, Komatsu Y, Roten L, Jadidi A, Linton N, Pedersen M, Daly M, O'neill M, Knecht S, Weerasooriya R, Rostock T, Manninger M, Cochet H, Shah AJ, Yeim S, Denis A, Derval N, Hocini M, Sacher F, Haissaguerre M, Jais P. Five-year outcome of catheter ablation of persistent atrial fibrillation using termination of atrial fibrillation as a procedural endpoint. *Circulation* 2015;8:18–24.
- Schreiber D, Rostock T, Fröhlich M, Sultan A, Servatius H, Hoffmann BA, Lüker J, Berner I, Schäffer B, Wegscheider K, Lezius S, Willems S, Steven D. Five-year follow-up after catheter ablation of persistent atrial fibrillation using the stepwise approach and prognostic factors for success. *Circulation* 2015;8:308–317.
- Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, Kim YH, Klein G, Natale A, Packer D, Skanes A. Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. J Am Coll Cardiol 2009;53:1798–1803.
- 7. Arbelo E, Brugada J, Hindricks G, Maggioni A, Tavazzi L, Vardas P, Anselme F, Inama G, Jais P, Kalarus Z, Kautzner J, Lewalter T, Mairesse G, Perez-Villacastin J, Riahi S, Taborsky M, Theodorakis G, Trines S. Esc-eurobservational research programme: the atrial fibrillation ablation pilot study, conducted by the European heart rhythm association. *Europace* 2012;**14**:1094–1103.
- Arbelo E, Brugada J, Hindricks G, Maggioni AP, Tavazzi L, Vardas P, Laroche C, Anselme F, Inama G, Jais P, Kalarus Z, Kautzner J, Lewalter T, Mairesse GH, Perez-Villacastin J, Riahi S, Taborsky M, Theodorakis G, Trines SA, Investigators otbotAFAPS. The atrial fibrillation ablation pilot study: an european survey on

methodology and results of catheter ablation for atrial fibrillation conducted by the european heart rhythm association. *Eur Heart J* 2014;**35**:1466–1478.

- Camm AJ, Kirchhof P, Lip GYH, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H, Alfieri O, Angelini A, Atar D, Colonna P, De Caterina R, De Sutter J, Goette A, Gorenek B, Heldal M, Hohloser SH, Kolh P, Le Heuzey J-Y, Ponikowski P, Rutten FH. Guidelines for the management of atrial fibrillation. *Eur Heart* J 2010;**31**:2369–2429.
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (strobe) statement: guidelines for reporting observational studies. *Lancet* 2007;**370**:1453–1457.
- 11. Tung R, Buch E, Shivkumar K. Catheter ablation of atrial fibrillation. *Circulation* 2012;**126**:223–229.
- Mont L, Bisbal F, Hernández-Madrid A, Pérez-Castellano N, Viñolas X, Arenal A, Arribas F, Fernández-Lozano I, Bodegas A, Cobos A, Matía R, Pérez-Villacastín J, Guerra JM, Ávila P, López-Gil M, Castro V, Arana JI, Brugada J, Investigators oboS. Catheter ablation vs. Antiarrhythmic drug treatment of persistent atrial fibrillation: a multicentre, randomized, controlled trial (sara study). *Eur Heart J* 2014;**35**:501–507.
- Kuck K-H, Brugada J, Fürnkranz A, Metzner A, Ouyang F, Chun KRJ, Elvan A, Arentz T, Bestehorn K, Pocock SJ, Albenque J-P, Tondo C. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. N Engl J Med 2016;374:2235–2245.
- 14. Lip GYH, Laroche C, Ioachim PM, Rasmussen LH, Vitali-Serdoz L, Petrescu L, Darabantiu D, Crijns HJGM, Kirchhof P, Vardas P, Tavazzi L, Maggioni AP, Boriani G. Prognosis and treatment of atrial fibrillation patients by European cardiologists: One year follow-up of the eurobservational research programmeatrial fibrillation general registry pilot phase (eorp-af pilot registry). *Eur Heart J* 2014;**35**:3365–3376.
- 15. Kirchhof P, Ammentorp B, Darius H, De Caterina R, Le Heuzey J-Y, Schilling RJ, Schmitt J, Zamorano JL. Management of atrial fibrillation in seven european countries after the publication of the 2010 esc guidelines on atrial fibrillation: Primary results of the prevention of thromboemolic events—European registry in atrial fibrillation (prefer in af). *Europace* 2014;**16**:6–14.
- 16. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen S-A, Crijns HJG, Damiano RJ, Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaguerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim Y-H, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky ER, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao H-M, Wilber ∧ D, Prystowsky EN, Damiano R, Jackman WM, Jalife J, Marchlinski F, McCarthy P, Wilber D, Ad N, Cummings J, Gillinov AM, Heidbuchel H, January C, Lip G, Markowitz S, Nair M, Ovsyshcher IE, Pak H-N, Tsuchiya T, Shah D, Siong TW, Vardas PE. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Europace* 2012;**14**:528–606.
- January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG,

Tchou PJ, Tracy CM, Yancy CW. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American college of cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation* 2014;**130**:e199–e267.

- Rienstra M, Lubitz SA, Mahida S, Magnani JW, Fontes JD, Sinner MF, Van Gelder IC, Ellinor PT, Benjamin EJ. Symptoms and functional status of patients with atrial fibrillation. *Circulation* 2012;**125**:2933–2943.
- Tamborero D, Mont L, Berruezo A, Matiello M, Benito B, Sitges M, Vidal B, de Caralt TM, Perea RJ, Vatasescu R, Brugada J. Left atrial posterior wall isolation does not improve the outcome of circumferential pulmonary vein ablation for atrial fibrillation: a prospective randomized study. *Circulation* 2009;**2**:35–40.
- Arbelo E, Guiu E, Ramos P, Bisbal F, Borras R, Andreu D, Tolosana JM, Berruezo A, Brugada J, Mont L. Benefit of left atrial roof linear ablation in paroxysmal atrial fibrillation: a prospective, randomized study. J Am Heart Assoc 2014;3:e000877.
- 21. Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Horton R, Gallinghouse GJ, Lakkireddy D, Verma A, Khaykin Y, Hongo R, Hao S, Beheiry S, Pelargonio G, Dello Russo A, Casella M, Santarelli P, Santangeli P, Wang P, Al-Ahmad A, Patel D, Themistoclakis S, Bonso A, Rossillo A, Corrado A, Raviele A, Cummings JE, Schweikert RA, Lewis WR, Natale A. Periprocedural stroke and management of major bleeding complications in patients undergoing catheter ablation of atrial fibrillation: The impact of periprocedural therapeutic international normalized ratio. *Circulation* 2010;**121**:2550–2556.
- 22. Lakkireddy D, Reddy YM, Di Biase L, Vanga SR, Santangeli P, Swarup V, Pimentel R, Mansour MC, D'avila A, Sanchez JE, Burkhardt JD, Chalhoub F, Mohanty P, Coffey J, Shaik N, Monir G, Reddy VY, Ruskin J, Natale A. Feasibility and safety of dabigatran versus warfarin for periprocedural anticoagulation in patients undergoing radiofrequency ablation for atrial fibrillation: results from a multicenter prospective registry. *J Am Coll Cardiol* 2012;**59**:1168–1174.
- 23. Lakkireddy D, Reddy YM, Di Biase L, Vallakati A, Mansour MC, Santangeli P, Gangireddy S, Swarup V, Chalhoub F, Atkins D, Bommana S, Verma A, Sanchez JE, Burkhardt JD, Barrett CD, Baheiry S, Ruskin J, Reddy V, Natale A. Feasibility and safety of uninterrupted rivaroxaban for periprocedural anticoagulation in patients undergoing radiofrequency ablation for atrial fibrillation: Results from a multicenter prospective registry. J Am Coll Cardiol 2014;**63**:982–988.
- 24. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener H-C, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P, Reviewers D, Agewall S, Camm J, Baron Esquivias G, Budts W, Carerj S, Casselman F, Coca A, De Caterina R, Deftereos S, Dobrev D, Ferro JM, Filippatos G, Fitzsimons D, Gorenek B, Guenoun M, Hohnloser SH, Kolh P, Lip GYH, Manolis A, McMurray J, Ponikowski P, Rosenhek R, Ruschitzka F, Savelieva I, Sharma S, Suwalski P, Tamargo JL, Taylor CJ, Van Gelder IC, Voors AA, Windecker S, Zamorano JL, Zeppenfeld K. 2016 ESC guidelines for the management of atrial fibrillation of the European society of cardiology (ESC)developed with the special contribution of the European heart rhythm association (EHRA) of the escendorsed by the European Stroke organisation (ESO). *Eur Heart J* 2016;**37**:2893–2962.