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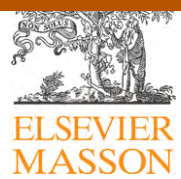

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CLINICAL RESEARCH

Characteristics and management of outpatients with history of or current atrial fibrillation: The observational French EPHA study☆

Caractéristiques et prise en charge des patients ambulatoires avec un antécédent ou en FA : étude observationnelle française EPHA

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KEYWORDS
Atrial fibrillation;
Outpatient;
Comorbidity;
Hospitalization;
Healthcare resource;
Therapeutic strategy

Summary
Background. — Limited French data are available for the different clinical types (paroxysmal, persistent and permanent) of atrial fibrillation and their comorbidities (AF).
Aims. — To provide contemporary insights into the characteristics and management of outpatients with a history of or current AF in France.
Methods. — EPHA is a national, observational, cross-sectional, multicentre descriptive study with retrospective data collection relating to the management, treatment and hospitalization of patients with AF.
Results. — One thousand three hundred and thirty-one patients (mean age: 74 ± 11 years [55.7% ≥ 75 years]; 58.8% men) were included into the study between February 2009 and May 2009; their data were collected during the past 12 months. Of these, 38.2% had paroxysmal AF,

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10.0% persistent AF and 51.8% permanent AF. Most patients had at least one cardiovascular risk factor (80.8%). Almost all patients (96.6%) had received an antiarrhythmic drug in the previous year, of which 59.6% received a rhythm control strategy (class I, class III) with or without rate control strategy (class II, class IV, digitalis) and 40.6% received a rate control strategy exclusively. Almost all (94.4%) patients were treated with an antithrombotic: 83.4% with a vitamin K antagonist and 21.9% with antiplatelet therapy. Almost one-fifth (18.4%) of patients had been hospitalized related to AF at least once in the previous year. Patients with paroxysmal and persistent AF were hospitalized more frequently (20.0% and 31.1%, respectively) than patients with permanent AF (14.8%).
Conclusions. — About half of the patients had paroxysmal or persistent AF. Four-fifths of AF patients had at least one cardiovascular risk factor. The use of antiarrhythmic and antithrombotic treatments was very high. The rhythm control strategy was preferred in patients with paroxysmal or persistent AF.

MOTS CLÉS
Fibrillation auriculaire ;
Patients ambulatoires ;
Comorbidité ;
Hospitalisation ;
Ressources médicales ;
Stratégie thérapeutique

Résumé
Introduction. — Il existe peu de données françaises sur les différents types cliniques de fibrillation auriculaire (FA) (paroxystique, persistante ou permanente) et leurs comorbidités.
Objectif. — Décrire les caractéristiques et la prise en charge des patients ambulatoires présentant un antécédent de FA ou actuellement en FA, en France.
Méthodes. — L'étude EPHA est une étude française, observationnelle, transversale, multicentrique descriptive avec recueil rétrospectif des données de prise en charge, de traitement et d'hospitalisation des patients atteints de FA.
Résultats. — Mille trois cent trente-et-un patients (âge moyen : 74 ± 11 ans [55,7 % ≥ 75 ans] ; 58,8 % de sexe masculin) ont été inclus dans l'étude entre février 2009 et mai 2009, les données ont été recueillies sur les 12 derniers mois. Parmi ces patients, 38,2 % avaient une FA paroxystique, 10 % une FA persistante et 51,8 % une FA permanente. La majorité de ces patients avait au moins un facteur de risque cardiovasculaire (80,8 %). La quasi-totalité des patients (96,6 %) étaient sous traitement antiarythmique dans l'année précédant l'inclusion. Parmi les patients traités, 59,6 % recevaient un traitement de contrôle du rythme (antiarythmiques de classe I ou III) avec ou sans traitement de contrôle de la fréquence cardiaque (antiarythmiques de classe II, de classe IV ou digitaliques) et 40,6 % recevaient exclusivement un traitement de contrôle de la fréquence cardiaque. La majorité des patients (94,4 %) recevaient un antithrombotique : 83,4 % un antivitamine K et 21,9 % un antiplaquettaire. Près d'un cinquième des patients (18,4 %) ont été hospitalisés au moins une fois pour raison cardiovasculaire liée à la FA dans l'année précédente. Les patients en FA paroxystique ou persistante ont plus souvent été hospitalisés (20,0 % et 31,1 %, respectivement) que les patients en FA permanente (14,8 %).
Conclusion. — Environ la moitié des patients avaient une FA paroxystique ou persistante. Quatre patients sur cinq en FA avaient au moins un facteur de risque cardiovasculaire. L'utilisation de traitements antiarythmiques et antithrombotiques était très élevée. Une stratégie de contrôle du rythme était plus fréquent chez les patients en FA paroxystique ou persistante que chez les patients en FA permanente. Ces résultats soulignent la nécessité de traitements ou techniques avec un meilleur rapport bénéfice—risque afin d'optimiser la prise en charge de cette pathologie dont la prévalence ne cesse de croître.

Introduction

Atrial fibrillation (AF) is the most frequently observed cardiac arrhythmia in clinical practice. It is a major cause of long-term morbidity and mortality including major cardiovascular events as ischaemic stroke, heart failure and all-cause death [1—3]. One in six strokes occurs in patients with AF [4], and mortality in these patients is about double that of subjects in sinus rhythm and is related directly to the severity of underlying heart disease [4].

The estimated prevalence of AF ranges from 0.4—1% in the general population, rising to 8% in patients older than 80 years [4,5]. AF affects around 2.2 million people in the United States and 4.5 million in Europe [6]; between 600,000 and one million patients in France are estimated to have AF [6—8]. These figures will escalate with the ageing of the population, leading to increasing healthcare expenses of AF management.

AF can be defined as paroxysmal (AF that terminates spontaneously and generally lasts ≤ 7 days), persistent (AF that does not terminate spontaneously and usually lasts > 7 days), and permanent (AF in which cardioversion has failed or has not been attempted). When a patient has had two or more episodes, AF is considered recurrent. The distribu-

tion of clinical AF types varies in France [9,10]. Permanent AF is diagnosed in 30—50% of AF cases, with paroxysmal or persistent AF accounting for the remaining 50—70%. To the best of our knowledge, there is no recent French epidemiological study describing the different types of AF and age, comorbidities and treatment. The Euro Heart Survey recently described treatment and prognosis up to 1 year, according to type of AF, in subjects in 35 European countries, but included only 51 patients from France [11,12].

The primary objective of the present study is to describe the distribution of clinical AF types in patients with a history of or current AF who were being followed-up by cardiologists in France. The secondary objectives are: to determine the patients' characteristics, cardiovascular risk factors, and comorbidities for each type of AF; to describe treatment strategies during the past year; to describe the cardiovascular hospitalizations related to AF and to its complications; and to estimate the healthcare resources consumed.

Methods

EPHA is a national, observational, cross-sectional, multicentre descriptive study with retrospective data collection relating to the management, treatment and hospitalization of patients with AF.

Physician selection

Three thousand cardiologists were identified at random from a comprehensive national database (TVF physician identification database) of all cardiologists in France. The aim was to enrol 300 physicians, 100 from hospital-based practices and 200 from office-based or both hospital- and office-based practices willing to participate in the study. Each cardiologist completed a standardized case report form that collected information about their age, sex, year of graduation, department of practice, type of practice (office- or hospital-based practice), mean number of patients seen each month, and mean number of patients seen each month with a history of or current documented AF.

The representativeness of the physician sample was checked by comparing the distribution of participating cardiologists with national statistics published by the Direction de la recherche, des études, de l'évaluation et des statistiques (DREES) [13], in order to verify the lack of selection biases. The physicians enrolled patients seen during the course of normal clinical practice and no changes were imposed by the study in the diagnosis and treatment of these individuals.

Patient selection

Investigating physicians undertook to include the first eight consecutive patients who fulfilled the inclusion criteria, until 1300 patients had been enrolled.

Men and women aged ≥ 18 years were eligible for inclusion if they had been seen in consultation, and monitored, by a cardiologist for at least 1 year; had a history of or current documented AF (on an electrocardiogram [ECG] or Holter ECG) for at least 1 year, irrespective of the rhythm on the day of inclusion; and provided written informed consent before participating in the study.

Patients were excluded from this study if they presented with AF due to a transient cause (e.g., thyrotoxicosis, excessive alcohol intake, myocarditis, pericarditis, acute myocardial infarction, pulmonary embolism, metabolic disturbances or electrocution), with AF following cardiac surgery within the past 3 months or had not been monitored regularly by the investigator (last visit > 12 months before inclusion).

Cardiologists completed case report forms that collected data on the patient's demographics, cardiovascular risk factors, medical history, clinical examination, characteristics of AF, electrocardiographic and echocardiographic data, biological data, management of AF during the past 12 months, and healthcare resources related to AF management (including number of hospitalizations related to AF). Direct healthcare resources only were considered.

Statistical methods

The sample size was determined in order to have a degree of precision ≥ 2.5% to describe the different types of AF, 1300 patients needed to be enrolled. For the statistical analysis, prespecified descriptive analyses were performed. These analyses (percentages and means) are based on the number of non-missing values for each variable. All categorical variables were tested between the three types of AF using chi-square, and continuous variables using analysis of variance.

The study protocol was submitted to two national authorities, Comité consultatif sur le traitement de l'information en matière de recherche dans le domaine de la santé (CCTIRS) and Commission nationale de l'informatique et des libertés (CNIL), and was conducted in accordance with French law and the declaration of Helsinki.

Results

Study population

Of 416 cardiologists who agreed to participate, 234 enrolled at least one patient into the study. A total of 1470 patients were enrolled between 25 February and 6 May 2009. Of these, 41 did not provide written informed consent and were excluded from the study. A further 98 did not fulfil the inclusion criteria. The analysis is therefore based on data from 1331 patients.

Patient characteristics at consultation

The characteristics of the 1331 patients included in the study are shown in Table 1. The mean age was 74 ± 11 years (55.7% were ≥ 75 years) and 58.8% were men. Over half of the 1331 patients enrolled had permanent AF (51.8%, 95% CI 49.2—54.5), 38.2% (95% CI 35.6—40.8) had paroxysmal AF and 10.0% (95% CI 8.4—11.6) had persistent AF. Younger patients were more likely to present paroxysmal or persistent AF, whereas older patients (≥ 75 years) more often presented permanent AF (Fig. 1).

Table 1 Patient demographics and characteristics overall and according to type of atrial fibrillation.

	Paroxysmal AF ($n = 508$)	Persistent AF ($n = 133$)	Permanent AF ($n = 690$)	p value[a]	Total ($n = 1331$)
Demographics					
Men	292 (57.5)	80 (60.2)	411 (59.6)	0.73	783 (58.8)
Age, years	71 ± 11	72 ± 11	76 ± 9	< 0.001	74 ± 11
≥ 75 years	221 (43.5)	64 (48.1)	457 (66.2)	< 0.001	742 (55.7)
Cardiovascular risk factors					
≥ 1 risk factor	406 (80.1)	108 (81.2)	560 (81.3)	0.87	1074 (80.8)
Hypertension	318 (78.3)	93 (86.1)	450 (80.4)	0.19	861 (80.2)
Diabetes mellitus	71 (17.5)	23 (21.3)	121 (21.6)	0.27	215 (20.0)
Dyslipidaemia	244 (60.1)	61 (56.5)	320 (57.3)	0.64	625 (58.3)
Smoking history					
Current	29 (7.1)	6 (5.6)	26 (4.7)	0.30	61 (5.7)
Stopped < 3 years	15 (3.7)	3 (2.8)	13 (2.3)		31 (2.9)
Stopped ≥ 3 years	107 (26.4)	38 (35.2)	163 (29.2)		308 (28.7)
Family history of premature CVD					
Paternal[b]	25 (7.4)	9 (11.3)	28 (6.6)	0.35	62 (7.4)
Maternal[c]	14 (4.1)	4 (5.0)	10 (2.4)	0.28	28 (3.3)
Early stroke (< 45 years)	4 (1.2)	4 (5.0)	1 (0.2)	0.003	9 (1.1)
No family history of premature CVD	301 (88.5)	66 (82.5)	386 (91.5)	0.0448	753 (89.4)
Medical history and comorbidities					
≥ 1 medical history/comorbidity	365 (72.0)	103 (77.4)	598 (87.0)	< 0.001	1066 (80.3)
Heart failure	65 (17.8)	29 (28.2)	250 (41.8)	< 0.001	344 (32.3)
NYHA class I	15 (23.1)	7 (24.1)	31 (12.5)	0.13	53 (15.5)
NYHA class II	39 (60.0)	15 (51.7)	170 (68.5)		224 (65.5)
NYHA class III	11 (16.9)	6 (20.7)	44 (17.7)		61 (17.8)
NYHA class IV	0	1 (3.4)	3 (1.2)		4 (1.2)
Ischaemic stroke	29 (7.9)	9 (8.7)	45 (7.5)	0.91	83 (7.8)
Transient ischaemic attack	31 (8.5)	5 (4.9)	40 (6.7)	0.37	76 (7.1)
Ischaemic heart disease	82 (22.5)	29 (28.2)	165 (27.6)	0.18	276 (25.9)
Non-ischaemic heart disease	101 (27.7)	25 (24.3)	200 (33.4)	0.058	326 (30.6)
Valvular disease	108 (29.6)	32 (31.1)	258 (43.1)	< 0.001	398 (37.3)
Rheumatic	18 (16.7)	6 (18.8)	71 (27.6)	0.063	95 (23.9)
Pulmonary disease	51 (14)	20 (19.4)	80 (13.4)	0.26	151 (14.2)
Thyroid disease	62 (17.0)	14 (13.6)	86 (14.4)	0.49	162 (15.2)
Hypothyroidism	51 (82.3)	9 (69.2)	60 (73.2)	0.36	120 (76.4)
Hyperthyroidism	11 (17.7)	4 (30.8)	22 (26.8)		37 (23.6)
Chronic renal insufficiency	30 (8.2)	7 (6.8)	54 (9.0)	0.73	91 (8.5)
Sleep apnea syndrome	27 (7.4)	10 (9.7)	40 (6.7)	0.54	77 (7.2)
Pacemaker	65 (17.8)	10 (9.7)	138 (23.1)	0.0032	213 (20.0)

Data given as n (%) or mean ± standard deviation.
CVD: cardiovascular disease; NYHA: New York Heart Association.
[a] Analysis of variance or chi-square.
[b] MI or sudden death before age 55 in father or parent of first-degree male relative.
[c] MI or sudden death before age 65 in mother or parent of first-degree female relative.

Cardiovascular risk factors, medical history and comorbidities

Most patients (80.8%) had at least one cardiovascular risk factor, including hypertension (80.2%), dyslipidaemia (58.3%), a history of or current tobacco consumption (37.3%), diabetes mellitus (20.0%) and a family history of premature cardiovascular disease (10.6%). The proportion of patients with at least one cardiovascular risk factor was

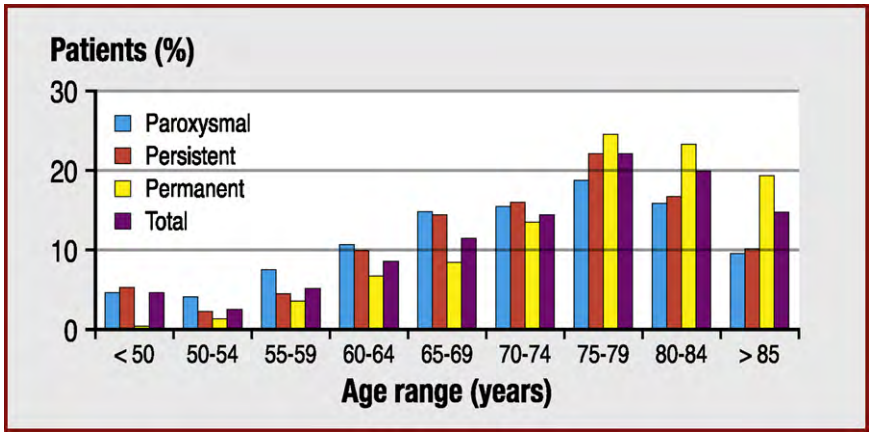

Figure 1. Age distribution for men and women enrolled in the EPHA study ($p < 0.001$ for trend).

similar irrespective of the type of AF (80.1% for paroxysmal, 81.2% for persistent, 81.3% for permanent) (Table 1).

Almost one-third of patients with AF had a history of heart failure, which was most frequent among the group with permanent AF (41.8% vs. 28.2% for persistent AF and 17.8% for paroxysmal AF, $p < 0.001$). Patients with permanent AF more often had New York Heart Association class III–IV heart failure (6.8%) compared to patients with paroxysmal or persistent AF (2.8%). Eight per cent had a history of ischaemic stroke; 25.9% had ischaemic heart disease; 30.6% had non-ischaemic heart disease; and 37.3% had valvular disease. Patients with permanent AF more often had valvulopathy (43.1%) compared to patients with persistent (31.1%) or paroxysmal (29.6%) AF; one-fifth of patients had a pacemaker.

Overall, 15.2% had thyroid disease, most commonly hypothyroidism (76.4%), and 8.5% had chronic renal insufficiency, but there was no significant difference in the prevalences across AF types.

$CHADS_2$ score at study entry

The mean $CHADS_2$ [14] (heart failure, hypertension, age ≥ 75 years, diabetes, stroke or transient ischaemic attack [TIA]) score was highest in patients with permanent AF, intermediate in those with persistent AF and lowest in patients with paroxysmal AF ($p < 0.001$) (Table 2). One-third of patients with permanent AF were at high risk of a stroke ($CHADS_2$ score > 2) vs. 27.8% of those with persistent AF and 17.1% with paroxysmal AF.

Overall, 71.6% of outpatients with AF were being managed for a long-term illness (i.e., France-specific, fully reimbursed condition or *affection de longue durée* [ALD]), 61.4% with paroxysmal AF, 60.9% with persistent AF, and 81.2% with permanent AF. The most frequent long-term illness was linked to a cardiovascular disease (89.1%).

Characteristics of the AF

The mean time since diagnosis of AF was 6.1 ± 5.3 years and differed significantly depending on AF type: 7.0 ± 5.5 years for permanent AF, 5.3 ± 5.0 years for paroxysmal AF and 4.9 ± 5.0 years for persistent AF ($p < 0.001$). The majority of patients had symptomatic AF (59.1%), with no differences by clinical type, whereas symptoms varied according to AF type: palpitations were most frequent in patients with paroxysmal or persistent AF; dyspnoea was more common in patients with permanent or persistent AF (Table 3).

Management in previous 12 months

Cardioversion

During the year before enrolment into the study, 12.1% of patients had undergone a cardioversion (pharmacological in 48.4%, electrical in 25.8%, both in 30.3%). The last attempted cardioversion had been successful in 74.1% of the patients and was least successful in patients with permanent AF (Table 4).

Pharmacological treatment

Almost all (96.6%) patients had received an antiarrhythmic drug in the previous year and 3.4% were not treated (Table 4). Among these treated patients, 40.6% of patients received a rate control strategy (class II, class IV, digitalis) exclusively; the remaining patients received either a rhythm control strategy (class I, class III) or both rhythm and rate control strategies. A rhythm control strategy (exclusively or with rate control strategy) was preferred in patients with paroxysmal AF (58% exclusively; 89,6% both) and in patients with persistent AF (44% exclusively; 75,4% both). A rate control strategy alone was preferred in patients with permanent AF (69.3% vs. 24.6% in persistent AF and 10.4% in paroxysmal AF; $p < 0.001$). The most frequently used antiarrhythmic drugs in the overall population were class II (41.2%), followed by amiodarone (32.5%) and class Ic sodium channel blockers (24.1%) (Table 4). Overall, 27.4% of patients had discontinued or changed of antiarrhythmic treatment over the previous 12 months, which was more frequently among paroxysmal (30%) and persistent (43%) than permanent (22%) AF patients ($p < 0.001$) (Table 4). The main reasons for therapy discontinuation were adverse events (40.9%) and therapeutic escape (40.9%).

At enrolment into the study, almost all (94.4%) patients were treated with an antithrombotic: 83.4% with a vitamin K antagonist and 21.9% with antiplatelet therapy (Table 4). Patients with permanent AF were more frequently treated with an antithrombotic (99.1%) than patients with

Table 2 Electrocardiogram, electrocardiography characteristics, physical and biological examination, according to type of atrial fibrillation.

	Paroxysmal AF ($n = 508$)	Persistent AF ($n = 133$)	Permanent AF ($n = 690$)	p value[a]	Total ($n = 1331$)
Reason for consultation					
AF monitoring	367 (72.7)	104 (78.8)	480 (70.3)	0.12	951 (72.0)
Other reason	122 (24.2)	23 (17.4)	165 (24.2)		310 (23.5)
Both	16 (3.2)	5 (3.8)	38 (5.6)		59 (4.5)
Mean time since diagnosis of AF (years)	5.3 (5.0)	4.9 (4.9)	7.0 (5.5)	< 0.001	6.1 (5.3)
Symptoms					
None	216 (43.1)	48 (36.1)	272 (40.1)	0.29	536 (40.9)
Palpitations	186 (37.1)	48 (36.1)	84 (12.4)	< 0.001	318 (24.2)
Dyspnoea	143 (28.5)	54 (40.6)	354 (52.2)	< 0.001	551 (42.0)
Asthenia	70 (14.0)	35 (26.3)	135 (19.9)	0.0014	240 (18.3)
Chest pain	27 (5.4)	5 (3.8)	20 (2.9)	0.10	52 (4.0)
Lipothymia	34 (6.8)	2 (1.5)	17 (2.5)	< 0.001	53 (4.0)
Syncope	4 (0.8)	0	1 (0.1)	0.23	5 (0.4)
Other	11 (2.2)	2 (1.5)	8 (1.2)	0.39	21 (1.6)
Physical examination					
BMI (kg/m^2)	26.6 ± 4.6	27.8 ± 5.7	27.04 ± 4.8	0.04	27.0 ± 4.9
$< 25\ kg/m^2$	203 (40.0)	38 (28.8)	244 (35.6)	0.10	485 (36.6)
$25—30\ kg/m^2$	199 (39.3)	60 (45.5)	270 (39.4)		529 (39.9)
$> 30\ kg/m^2$	105 (20.7)	34 (25.8)	172 (25.1)		311 (23.5)
Systolic BP (mmHg)	136.8 ± 16.3)	138.5 ± 17.5	134.0 ± 15.4	0.001	135.5 ± 16.0
Diastolic BP (mmHg)	77.4 ± 9.2	79.5 ± 9.7	77.3 ± 8.8	0.03	77.6 ± 9.0
ECG characteristics					
Sinus rhythm	423 (85.3)	59 (45.0)	0		482 (37.0)
AF	38 (7.7)	65 (49.6)	637 (94.1)		740 (56.7)
Atrial flutter	5 (1.0)	3 (2.3)	20 (3.0)		28 (2.1)
Heart rate (bpm)	66.4 ± 14.1	76.8 ± 20.6	74.5 ± 13.6	< 0.001	71.6 ± 15.2
QT (ms)	380.7 ± 108.1	347.4 ± 136.1	346.0 ± 122.1	< 0.001	360.3 ± 119.4
LVH	52 ± 10.9	12 ± 9.4	87 ± 13.8	0.21	151 ± 12.2
Sokoloff index	22.7 ± 8.8	23.1 ± 9.8	23.6 ± 9.5	0.32	23.2 ± 9.3
Negative T wave	94 (19.3)	27 (21.6)	223 (34.5)	< 0.001	344 (27.3)
Echocardiography	386 (76.0)	109 (82.0)	519 (75.2)	< 0.001	1014 (76.3)
Mean time since echocardiography, days	99.31 ± 110.32	93.86 ± 97.83	89.54 ± 104.21	0.40	93.71 ± 105.92
Diameter of left atrium, mm (mean)	40.99 ± 7.31	43.19 ± 7.47	47.81 ± 8.72	< 0.001	44.72 ± 8.69
Surface area of left atrium, cm^2 (mean)	23.33 ± 7.87	25.56 ± 8.25	30.27 ± 10.42	< 0.001	27.15 ± 9.87
LVEF, % (mean)	62.81 ± 11.08	60.74 ± 11.50	58.02 ± 12.45	< 0.001	60.12 ± 12.05
Shortening fraction, % (mean)	36.37 ± 9.06	34.86 ± 8.14	33.14 ± 9.37	< 0.001	34.55 ± 9.24
Biological examination					
Creatininaemia (mean), µmol/L	98.38 ± 38.93	96.15 ± 31.37	101.25 ± 43.34	0.40	99.65 ± 40.64
Kalaemia, meq/L	4.30 ± 0.40	4.28 ± 0.48	4.37 ± 0.44	0.04	4.33 ± 0.43
INR (mean)	2.33 ± 0.64	2.51 ± 0.79	2.53 ± 0.61	< 0.001	2.47 ± 0.65

Data given as number (%) or mean ± SD unless otherwise stated.
AF: atrial fibrillation; ECG: electrocardiogram; LVEF: left ventricular ejection fraction; INR: international normalized ratio; LVH: left ventricular hypertrophy; MI: myocardial infarction.
[a] Chi-square or analysis of variance.

Table 3 $CHADS_2$ score overall and according to type of atrial fibrillation.

	Paroxysmal AF ($n = 508$)	Persistent AF ($n = 133$)	Permanent AF ($n = 690$)	p value[a]	Total ($n = 1331$)
$CHADS_2$ score	1.49 ± 1.13	1.72 ± 1.29	2.04 ± 1.20	< 0.001	1.80 ± 1.21
0	100 (19.7)	29 (21.8)	64 (9.3)	< 0.001	193 (14.5)
1	177 (34.8)	29 (21.8)	170 (24.6)		376 (28.2)
2	144 (28.3)	38 (28.6)	233 (33.8)		415 (31.2)
> 2	87 (17.1)	37 (27.8)	223 (32.3)		347 (26.1)

[a] Chi-square or analysis of variance.

Table 4 Management of atrial fibrillation overall and according to type of atrial fibrillation.

	Paroxysmal AF ($n = 508$)	Persistent AF ($n = 133$)	Permanent AF ($n = 690$)	p value[a]	Total ($n = 1331$)
Cardioversion in the past year	74 (14.6)	40 (30.5)	46 (6.7)	< 0.001	160 (12.1)
Number	1.1 (0. 5)	1.2 (0.4)	1.2 (0.5)	0.49	1.2 (0.4)
Type of cardioversion					
Electrical	20 (27.0)	10 (26.3)	10 (23.3)	0.90	40 (25.8)
Pharmacological	42 (56.8)	18 (47.4)	15 (34.9)	0.07	75 (48.4)
Pharmacological followed by electrical	14 (18.9)	12 (31.6)	21 (48.8)	0.003	47 (30.3)
Success of last attempted cardioversion	65 (92.9)	31 (91.2)	13 (30.2)	< 0.001	109 (74.1)
Antiarrhythmic treatment 12 months before enrolment	480 (97.6)	118 (95.2)	573 (96.1)	0.28	1171 (96.6)
Class Ia	10 (2.1)	1 (0.8)	1 (0.2)	0.007	12 (1.0)
Class Ib	1 (0.2)	0	0	0.51	1 (0.1)
Class Ic	211 (44.0)	37 (31.4)	34 (5.9)	< 0.001	282 (24.1)
Class II (beta-blocker)	149 (31.0)	46 (39.0)	288 (50.3)	< 0.001	483 (41.2)
Class III (potassium channel blocker)					
Sotalol	53 (11.0)	6 (5.1)	24 (4.2)	< 0.001	83 (7.1)
Amiodarone	199 (41.5)	54 (45.8)	128 (22.3)	< 0.001	381 (32.5)
Other	0	0	7 (1.2)	0.031	7 (0.6)
Class IV (calcium channel blocker)	21 (4.4)	9 (7.6)	46 (8.0)	0.049	76 (6.5)
Digitalis (digoxin)	43 (9.0)	20 (16.9)	269 (46.9)	< 0.001	332 (28.4)
Types of treatment 12 months before enrolment				< 0.001	
Rate control	50 (10.4)	29 (24.6)	397 (69.3)		476 (40.6)
Rhythm control	278 (57.9)	52 (44.1)	81 (14.1)		411 (35.1)
Both	152 (31.7)	37 (31.4)	95 (16.6)		284 (24.3)
Discontinuation or change of antiarrhythmic treatment	146 (29.7)	54 (43.5)	128 (22)	< 0.001	328 (27.4)
Reason: adverse events	57 (39.0)	18 (33.3)	59 (46.1)	0.23	134 (40.9)
Reason: therapeutic escape	68 (46.6)	28 (51.9)	38 (29.7)	0.004	134 (40.9)
Treatments taken at enrolment					
Antithrombotic	450 (88.6)	123 (92.5)	684 (99.1)	< 0.001	1257 (94.4)
Vitamin K antagonist	309 (68.7)	103 (84.4)	635 (93.0)	< 0.001	1047 (83.4)
Antiplatelet	159 (35.3)	21 (17.2)	95 (13.9)	< 0.001	275 (21.9)
Antihypertensive	356 (70.1)	103 (77.4)	538 (78.1)	0.005	997 (75.0)
Hypolipaemic	230 (45.5)	60 (45.1)	327 (47.7)	0.69	617 (46.6)

[a] Chi-square or analysis of variance.

paroxysmal (88.6%) or persistent (92.5%) AF ($p < 0.001$). Three-quarters of the patients were treated with antihypertensive therapy. The main antihypertensive treatments were: diuretics (55.3%), angiotensin II receptor antagonist (40.3%), beta-blockers (38.7%) and ACE inhibitors (37.3%). Almost half (46.6%) of the patients were treated with hypolipaemics, mainly statins (85.8%).

Healthcare resource consumption

Patients with paroxysmal or persistent AF had more consultations with a specialist and more cardiovascular hospitalizations related to AF and to its complications, compared to patients with permanent AF (Table 5). A total of 242 patients (18.4%) had been hospitalized at least once for AF in the previous year: patients with persistent and paroxysmal AF were hospitalized more frequently (31.1% and 20.0%, respectively) than patients with permanent AF (14.8%). Among hospitalized patients, 78.7% ($n = 188$ patients) were hospitalized at least once in an inpatient setting ($n = 241$ hospitalizations) and 37.6% ($n = 91$ patients) were hospitalized at least once in an outpatient setting ($n = 108$ hospitalizations). The most common reasons for inpatient hospitalization were for an arrhythmia or conduction disorder (24.2%), heart failure (23.8%), management with a pacemaker, defibrillator or other disposable intracardiac device (12.9%), and radiofrequency or surgical ablation (11.3%). The most common reason for outpatient hospitalization was for external electric shock (49.5%).

Discussion

This observational study provides insights into the characteristics and management of a contemporary population of outpatients with either a history of or current AF in France. Over half (52%) of the patients presented with permanent AF and 48% with paroxysmal or persistent AF. Cardiovascular risk factors were present in 80% of patients, with a high prevalence of hypertension and dyslipidaemia. The majority of patients had received an antiarrhythmic treatment in the previous 12 months, with a rate control strategy exclusively preferred in 40.6%.

Patients in this French registry were older and generally sicker than those in other observational studies of AF, with higher prevalences of hypertension, dyslipidaemia and stroke/transient ischaemic attack [10,12,15,16]. The rate of rheumatic heart disease was much higher (23.9%) than reported in the French *Étude en activité libérale de la fibrillation auriculaire* (ALFA; based on 1994 data) or German AFNET (Central Registry of the German Competence NETwork on Atrial Fibrillation; based on 2004–2006 data) (15.2% and 2.5–5.3%, respectively) study, but was similar to that reported in the Euro Heart Survey (21%) [12]. The higher proportion of valvular AF included in our series could explain the higher rate of cardioversion and concomitant treatments, including antithrombotics.

Antiarrhythmic treatment

Current guidelines from the American College of Cardiology/American Heart Association/European Society of Cardiology [4] recommend that the choice of a rate vs. rhythm control strategy should be guided by the patient's symptoms, as rhythm control has shown no survival benefit over rate control [17–25], and places patients at higher risk of drug-related adverse events [17,18,21] and hospitalizations [21,23]. According to the French Haute Autorité de santé (HAS) for AF management [5], prevention of cardiovascular events and reduction in cardiovascular mortality are the main priorities for physicians. However, class I and III antiarrhythmic drugs have never demonstrated a cardiovascular morbidity–mortality benefit in patients with AF [17,26,27].

The use of antiarrhythmic therapy was very high in the present study, with over 95% of patients having received some form of treatment across all AF categories in the previous 12 months. French physicians showed an overall preference for a rhythm control strategy, with or without rate control (59.4%), over a rate control strategy exclusively (40.6%) in AF management. When broken down by type of AF, physicians opted for rhythm control in patients with paroxysmal AF and for rate control in those with permanent AF, who were generally older, as recommended in the guidelines [4]. In the Euro Heart Survey of AF, in patients with current AF symptoms, a rhythm control strategy was applied to 67% of patients and a rate control strategy exclusively in 27% [12]. Similarly, in the German AFNET study, 63.4% of patients received a combination of rhythm and rate control drugs; 21.3% of patients were given rhythm control drugs (classes I and III), mainly those with paroxysmal or persistent AF [15]. In the Registry on cardiac rhythm disorders assessing the control of atrial fibrillation (RecordAF) [28] conducted in patients with recently diagnosed paroxysmal/persistent AF, rhythm- and rate-control strategies were applied to 55% and 45% of patients, respectively, at study inclusion. In France, the use of rhythm-control strategies was approximately double that of rate-control strategies. Class III drugs and beta-blockers were the most common AF medications prescribed at baseline. While the proportion of patients in the present study, treated exclusively with rhythm control therapies, was higher, at 35.1%, the pattern of prescribing was similar.

Antithrombotic therapy

Prevention of thrombotic events remains a public health high priority in patients with AF. Clinical risk stratification is recommended to identify those at intermediate to high risk of stroke [4]. Patients at high risk should receive warfarin with an international normalized ratio in the range of 2–3 (target 2.5) and those at low risk should receive aspirin [4]. The optimal strategy for patients at intermediate risk remains the subject of debate, with inconsistency between guidelines [4,29], but antithrombotic treatment with either aspirin or warfarin is recommended by the ACC/AHA/ESC 2006 guidelines [4] and the ACCP [30]. In a recent retrospective study, the administration of an anticoagulant in patients at intermediate risk of stroke ($CHADS_2$ score = 1) was associated with a lower rate of events compared with no anticoagulant treatment (relative risk 0.42, 95% confidence interval 0.29–0.60, $p < 0.0001$), whereas no such association was present for patients treated with an antiplatelet [31].

Table 5 Healthcare resource consumption related to AF, to its management and to its complications, in past 12 months.

Resources	Paroxysmal AF ($n=508$)	Persistent AF ($n=133$)	Permanent AF ($n=690$)	p value[a]	Total ($n=1331$)
Number of consultations related to AF (specialist)	3.0 ± 2.2	3.5 ± 2.7	2.6 ± 2.0	< 0.001	2.9 ± 2.1
Number of consultations related to AF (general practitioner)	5.1 ± 4.0	4.7 ± 3.7	5.4 ± 4.1	0.09	5.2 ± 4.0
≥ 1 outpatient investigation	494 (97.8)	131 (98.5)	669 (97.7)	0.84	1294 (97.8)
Hospitalization					
Patients with at least one hospitalization	100 (20.0)	41 (31.1)	101 (14.8)	< 0.001	242 (18.4)
In outpatient setting	37 (37.0)	21 (51.2)	33 (32.7)	0.12	91 (37.6)
In inpatient setting	80 (82.5)	30 (73.2)	78 (77.2)	0.43	188 (78.7)
Number of outpatient hospitalizations	48	21	39		108
Reasons for outpatient hospitalization					
External electric shock	20 (42.6)	15 (71.4)	18 (46.2)		53 (49.5)
Other	26 (55.3)	6 (28.6)	19 (48.7)		51 (47.7)
Multiple ticks	1 (2.1)	0	2 (5.1)		3 (2.8)
Number of inpatient hospitalizations	101	38	102		241
Primary reason of inpatient hospitalization					
Hypertension	0	1 (2.6)	0		1 (0.4)
Stable angina or atypical chest pain	2 (2.0)	0	3 (3.0)		5 (2.1)
Unstable angina or myocardial infarction	0	0	2 (2.0)		2 (0.8)
Heart failure	14 (13.9)	5 (13.2)	38 (37.6)		57 (23.8)
Cardiovascular surgery	1 (1.0)	1 (2.6)	3 (3.0)		5 (2.1)
Interventional procedure (arterial vascular access)	2 (2.0)	0	3 (3.0)		5 (2.1)
Arrhythmia or conduction disorder	33 (32.7)	17 (44.7)	8 (7.9)		58 (24.2)
Syncope	2 (2.0)	0	3 (3.0)		5 (2.1)
Non-fatal cardiac arrest	0	0	2 (2.0)		2 (0.8)
Placement of a pacemaker, defibrillator or intracardiac device	14 (13.9)	0	17 (16.8)		31 (12.9)
Radiofrequency or surgical ablation	17 (16.8)	7 (18.4)	3 (3.0)		27 (11.3)
Ischaemic stroke	2 (2.0)	1 (2.6)	3 (3.0)		6 (2.5)
Transient ischaemic attack	1 (1.0)	0	1 (1.0)		2 (0.8)
Symptomatic PAD	2 (2.0)	0	0		2 (0.8)
Major bleed	1 (1.0)	0	3 (3.0)		4 (1.7)
Adverse events of AF treatments	4 (4.0%)	2 (5.3%)	3 (3.0%)		9 (3.8%)
Other	6 (5.9)	4 (10.5)	9 (8.9)		19 (7.9)

Data given as number (%) or mean ± SD.
[a] Chi-square, analysis of variance or Fisher's exact test.

In the present study, 26.1% of patients were at moderate to high risk of stroke ($CHADS_2 > 2$). Despite this observation, 94.4% of patients received an antithrombotic (83.4% a vitamin K antagonist and 21.9% an antiplatelet). The overall use of antithrombotic therapy, driven by vitamin K antagonists, was highest among patients with permanent AF, and reflected the rising $CHADS_2$ score among these patients. In the German AFNET study, the proportion of patients at moderate to high risk of stroke ($CHADS_2$ score ≥ 2 in 38.8% with paroxysmal, 53.4% with persistent and 62.1% with permanent AF) was broadly similar, and the overall rate of use of antithrombotic medications was also comparable to that in the present study. The rates of use of oral anticoagulants were 55.6% for paroxysmal AF, 74.4% for persistent AF and 70.7% for permanent AF. Corresponding data from the present study were 93.0%, 84.4% and 68.7%. The Euro Heart Survey also reported lower rates of use of oral anticoagulant therapy (51%, 80%, 76%) [12].

Hospitalizations and healthcare use

On average AF resulted in 2.9 visits to the specialist and 5.2 visits to the GP per year and 348 hospitalizations for 1331 patients. According to a US study, AF is the most common cause of hospitalization for arrhythmia [32]. The risk of hospitalization in AF patients is more than double that of patients in sinus rhythm [33]. In the Euro

Heart Survey, between 30% and 43% of patients with AF were hospitalized for a cardiovascular reason during 1-year follow up [11]. In the COCAF study, 31.3% of patients were hospitalized over a mean follow-up of 329 ± 120 days [9]. The most frequent reasons for hospitalization in the COCAF study were for cardioversion, heart failure, pacemaker implantation or revision. In the present study, 18.4% of patients were hospitalized at least once for an AF-related cardiovascular reason in the preceding 12 months; this rate is for sure under-estimated, considering that data were collected retrospectively. It is important to note that patients with persistent and paroxysmal AF were hospitalized more frequently (31.1% and 20.0%, respectively) than patients with permanent AF (14.8%). Moreover, the average number of hospitalizations per patient was 1.5 for paroxysmal AF, 1.4 for persistent AF and 1.4 for permanent AF, illustrating the homogeneous burden of AF. As a matter of fact, the rate of hospitalization (average number of hospitalizations per patient × rate of patients with at least one hospitalization) was 30% for paroxysmal AF, 44.5% for persistent AF and 21% for permanent AF. The most frequent reasons for inpatient hospitalization were for heart failure or an arrhythmia or conduction disorder.

Study limitations

This study is subject to certain limitations, including the lack of longitudinal follow-up data due to the retrospective data collection. To minimize recruitment bias, cardiologists were identified at random from a comprehensive national database. Patient selection bias was diminished by enrolling the first eight consecutive patients who fulfilled the study criteria. However, owing to the retrospective design of this study a recruitment bias towards healthier AF patients is likely. While AF was classified as paroxysmal, persistent or permanent, follow-up at a later stage may provide additional data or re-classification that will impact on the optimal treatment strategy. Owing to the nature of the study, we are unable to comment on the antiarrhythmic strategy chosen in relation to the patients' clinical characteristics.

Conclusions

These observational data provide a recent perspective of AF care and comorbidities in France. One in two patients had paroxysmal or persistent AF, and four-fifths had at least one cardiovascular risk factor. The rhythm control strategy was preferred in patients with paroxysmal or persistent AF. The use of antiarrhythmic and antithrombotic treatments was very high, suggesting that French physicians are aware of the need for such therapies in the AF population.

Conflict of interest statement

Ariel Cohen works as an expert in scientific committees and advisory boards for sanofi-aventis, Bohringer, Astra-Zeneca, Bayer, Servier, and Novartis.

Jean Dallongeville works as an expert in scientific committees and advisory boards for sanofi-aventis, Astra-Zeneca, MSD, and Schering Plough.

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Stéphane Bouée is employed by CEMKA, which received a grant from sanofi-aventis to conduct the study and works with Astra-Zeneca, Merck Lipha, Roche, GlaxoSmithKline, Shire, Novartis, Sanofi Pasteur MSD, Nycomed, and Bristol-Myers-Squibb.

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