European Heart Journal (2014) **35**, 3365–3376
doi:10.1093/eurheartj/ehu374

Prognosis and treatment of atrial fibrillation patients by European cardiologists: One Year Follow-up of the EURObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase (EORP-AF Pilot registry)

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Received 30 June 2014; revised 21 July 2014; accepted 15 August 2014; online publish-ahead-of-print 31 August 2014

See page 3326 for the editorial comment on this article (doi:10.1093/eurheartj/ehu415)

Background The EURObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase (EORP-AF Pilot) provides systematic collection of contemporary data regarding the management and treatment of 3119 subjects with AF from 9 member European Society of Cardiology (ESC) countries. In this analysis, we report the development of symptoms, use of antithrombotic therapy and rate vs. rhythm strategies, as well as determinants of mortality and/or stroke/transient ischaemic attack (TIA)/peripheral embolism during 1-year follow-up in this contemporary European registry of AF patients.

Methods The registry population comprised consecutive in- and out-patients with AF presenting to cardiologists in participating ESC countries. Consecutive patients with AF documented by ECG were enrolled. Follow-up was performed by the local investigator, initially at 1 year, as part of a long-term cohort study.

Results At the follow-up, patients were frequently asymptomatic (76.8%), but symptoms are nevertheless common among paroxysmal and persistent AF patients, especially palpitations, fatigue, and shortness of breath. Oral anticoagulant (OAC) use remains high, ~78% overall at follow-up, and of those on vitamin K antagonist (VKA), 84% remained on VKA during the follow-up, while of those on non-VKA oral anticoagulant (NOAC) at baseline, 86% remained on NOAC, and 11.8% had changed to a VKA and 1.1% to antiplatelet therapy. Digitalis was commonly used in paroxysmal AF patients. Of rhythm control interventions, electrical cardioversion was performed in 9.7%, pharmacological cardioversion in 5.1%, and catheter ablation in 4.4%. Despite good adherence to anticoagulation, 1-year mortality was high (5.7%), with most deaths were cardiovascular (70%). Hospital readmissions were common, especially for atrial tachyarrhythmias and heart failure. On multivariate analysis, independent baseline predictors for mortality and/or stroke/TIA/peripheral embolism were age, AF as primary presentation, previous TIA, chronic kidney disease, chronic heart failure, malignancy, and

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minor bleeding. Independent predictors of mortality were age, chronic kidney disease, AF as primary presentation, prior TIA, chronic obstructive pulmonary disease, malignancy, minor bleeding, and diuretic use. Statin use was predictive of lower mortality.

Conclusion In this 1-year follow-up analysis of the EORP-AF pilot general registry, we provide data on the first contemporary registry focused on management practices among European cardiologists, conducted since the publication of the new ESC guidelines. Overall OAC use remains high, although persistence with therapy may be problematic. Nonetheless, continued OAC use was more common than in prior reports. Despite the high prescription of OAC, 1-year mortality and morbidity remain high in AF patients, particularly from heart failure and hospitalizations.

Keywords Atrial fibrillation • Stroke • Mortality • Prognosis • Registry

Introduction

Atrial fibrillation (AF) is the commonest sustained cardiac rhythm disorder, and many recent large randomized clinical trials have informed its management, with updated recommendations in guidelines and clinical practice protocols.[1] While representing the strongest evidence comparing therapy options and/or management strategies, clinical trials can be limited by the particular trial inclusion/exclusion criteria as well as the intervention(s) tested.[2] For example, the original historical trials of stroke prevention in AF conducted 20 years ago only randomized <10% of patients screened, and many stroke risk factors were neither recorded nor consistently defined.[3] Even contemporary stroke prevention trials with non-valvular AF have excluded patients with severe renal impairment and significant valvular heart disease, and information on managing such patients is needed from observational data. Thus, clinical trial data are complemented by large well-conducted 'real-world' registries that provide information particularly on clinical epidemiology and current treatment options used.

A decade ago, the European Society of Cardiology (ESC) conducted the EuroHeart survey series of registries to understand management strategies among European cardiologists. Substantial advances in new treatment options and new ESC guidelines suggest that treatment patterns may have changed since the EuroHeart survey on AF was conducted a decade ago.[4] The EURObservational Research Programme - Atrial Fibrillation General Registry Pilot Phase (EORP-AF Pilot) provides systematic collection of contemporary data regarding the management and treatment of 3119 subjects with AF from 9 member ESC countries, and baseline data have recently been reported.[5,6]

The EORP-AF pilot general registry was designed as a long-term cohort. The main objectives of the follow-up of the EORP-AF registry are as follows: (i) to obtain contemporary information on the occurrence of AF-related complications in Europe; (ii) to assess whether the diagnostic work-up of AF complies with current ESC guidelines (2010 guidelines[7] and the 2012 focused update[1]), and the impact on outcomes; (iii) to evaluate appropriateness of treatment in the different subsets of AF in relation to the current guidelines on AF, and the impact on outcomes; (iv) to describe the use of new antiarrhythmic therapy options such as catheter ablation and newly available antiarrhythmic drugs, and the impact on outcomes; and others.

In the current analysis, we present the 1-year data from the EORP-AF Pilot Registry, specifically focusing on symptoms, use of antithrombotic therapy, and rate vs. rhythm strategies, as well as determinants of mortality and stroke.

Methods

The methods and baseline data from the EORP-AF pilot general registry have previously been published.[5] The registry was commenced in early 2012. One-year follow-up phase ('pilot phase' or Phase 1) data were focused on the initial 3119 patients from 9 countries (for a broad representation of ESC member countries) recruited into this data set.

In brief, the registry population comprises consecutive in- and outpatients presenting with AF to cardiologists, enrolled in 67 centres in 9 countries.[5] Consecutive patients will be screened at the time of their presentation to a cardiologist (hospital or medical centre), and potential patients will be approached to obtain written informed consent according to the local rules. Enrolment required ECG-confirmed diagnosis of AF, with a qualifying episode of AF documented in the 12 months prior to enrolment. An ECG would be performed at (initially) 1 year (which may be repeated annually). Investigator sites chosen were a broad mix of tertiary and general hospitals, with and without capacity to perform cardiovascular surgery or electrophysiological interventions.

Follow-up was performed by the local cardiologist investigator, initially at 1 year, and will be repeated annually thereafter for two further years for Phase 1 (a total of 4 years). End-points of interest were mortality, stroke/thrombo-embolism, cardiovascular comorbidities, and hospital readmissions. For this analysis, we focused on 1-year outcomes. Stroke risk was categorized using the CHA_2DS_2-VASc score,[8] used within the ESC guidelines—for this analysis, 'low risk' was defined as CHA_2DS_2-VASc score = 0 (male) or 1 (female), 'moderate risk' was defined as CHA_2DS_2-VASc score = 1 (males) and 'high risk' as CHA_2DS_2-VASc score ≥2. Bleeding risk was categorized using the HAS-BLED score,[9] used within the ESC guidelines.

Statistical analyses

Univariate analysis was applied to both continuous and categorical variables. Continuous variables were reported as mean ± SD and/or as median and inter-quartile range (IQR). Among-group comparisons were made using a non-parametric test (Kruskal–Wallis test). Categorical variables were reported as percentages. Among-group comparisons were made using a χ^2 test or Fisher's exact test if any expected cell count was <5.

Plots of the Kaplan–Meier curves for time to all-cause death in relation to AF subtype were performed. The survival distributions between the type of AF have been compared using the log-rank test. All the variables at entry which were statistically significant at univariate analysis and variables considered of relevant clinical interest were included in the

Table 1 **Patient demography in relation to clinical subtype of atrial fibrillation**

	Total	First detected	Paroxysmal	Persistent	Long-standing persistent AF	Permanent	*P*-value
Age (years) (mean ± SD)	68.7 ± 11.6 ($n = 2589$)	68.4 ± 12.4 ($n = 774$)	66.7 ± 11.4 ($n = 693$)	67.9 ± 11.0 ($n = 550$)	70.9 ± 10.8 ($n = 121$)	73.0 ± 10.2 ($n = 451$)	<0.0001**
Age (years) [Median (IQR)]	69.0 (62.0–77.0) ($n = 2589$)	70.0 (61.0–77.0) ($n = 774$)	67.0 (60.0–75.0) ($n = 693$)	69.0 (61.0–75.0) ($n = 550$)	69.0 (63.0–79.0) ($n = 121$)	74.0 (66.0–81.0) ($n = 451$)	
Age (years, %)							
≤65	36.5 (945/2589)	36.3 (281/774)	44.2 (306/693)	39.5 (217/550)	29.8 (36/121)	23.3 (105/451)	<0.0001*
>65	63.5 (1644/2589)	63.7 (493/774)	55.8 (387/693)	60.5 (333/550)	70.2 (85/121)	76.7 (346/451)	
Gender (%)							
Male	60.6 (1568/2589)	64.2 (497/774)	58.4 (405/693)	60.4 (332/550)	61.2 (74/121)	57.6 (260/451)	0.1232*
Female	39.4 (1021/2589)	35.8 (277/774)	41.6 (288/693)	39.6 (218/550)	38.8 (47/121)	42.4 (191/451)	
CHA_2DS_2-VASc (%)							
Low risk	8.3 (215/2589)	7.5 (58/774)	13.9 (96/693)	7.6 (42/550)	3.3 (4/121)	3.3 (15/451)	<0.0001*
Moderate risk	10.5 (273/2589)	11.9 (92/774)	13.1 (91/693)	11.1 (61/550)	8.3 (10/121)	4.2 (19/451)	
High risk	81.2 (2101/2589)	80.6 (624/774)	73.0 (506/693)	81.3 (447/550)	88.4 (107/121)	92.5 (417/451)	
HAS-BLED Score class (%)							
0–2	86.0 (2227/2589)	85.7 (663/774)	89.3 (619/693)	86.9 (478/550)	79.3 (96/121)	82.3 (371/451)	0.0024*
3 or more	14.0 (362/2589)	14.3 (111/774)	10.7 (74/693)	13.1 (72/550)	20.7 (25/121)	17.7 (80/451)	
Follow-up duration (days) (mean ± SD)	366.4 ± 31.8 ($n = 2421$)	367.6 ± 30.2 ($n = 705$)	365.9 ± 32.6 ($n = 663$)	366.6 ± 29.3 ($n = 522$)	362.6 ± 22.6 ($n = 114$)	365.8 ± 37.6 ($n = 417$)	<0.0001**
Follow-up duration (days) [median (IQR)]	366.0 (359.0–378.0) ($n = 2421$)	367.0 (359.0–379.0) ($n = 705$)	365.0 (358.0–377.0) ($n = 663$)	367.0 (361.0–379.0) ($n = 522$)	363.0 (357.0–367.0) ($n = 114$)	369.0 (362.0–382.0) ($n = 417$)	
Current symptoms at 1-year follow-up (%)	23.2 (562/2423)	17.6 (124/705)	24.8 (165/665)	27.8 (145/522)	14.9 (17/114)	26.6 (111/417)	<0.0001*
Palpitations (%)	65.3 (367/562)	62.1 (77/124)	77.0 (127/165)	65.5 (95/145)	52.9 (9/17)	53.2 (59/111)	0.0008*
Dizziness (%)	18.7 (105/562)	26.6 (33/124)	18.2 (30/165)	14.5 (21/145)	23.5 (4/17)	15.3 (17/111)	0.0940*
General non-wellbeing (%)	30.4 (171/562)	33.9 (42/124)	31.5 (52/165)	31.0 (45/145)	47.1 (8/17)	21.6 (24/111)	0.1307*
Fatigue (%)	50.0 (281/562)	58.1 (72/124)	41.8 (69/165)	47.6 (69/145)	64.7 (11/17)	54.1 (60/111)	0.0375*
Shortness of breath (%)	43.1 (242/562)	39.5 (49/124)	38.2 (63/165)	46.2 (67/145)	70.6 (12/17)	45.9 (51/111)	0.0763*
Chest pain (%)	11.7 (66/562)	10.5 (13/124)	13.9 (23/165)	10.3 (15/145)	29.4 (5/17)	9.0 (10/111)	0.1281*
Fear/anxiety (%)	12.1 (68/562)	12.1 (15/124)	14.5 (24/165)	12.4 (18/145)	17.6 (3/17)	7.2 (8/111)	0.4154*
Other (%)	4.8 (27/562)	3.2 (4/124)	6.1 (10/165)	4.1 (6/145)	5.9 (1/17)	5.4 (6/111)	0.8237*

This table is focused on 2589 patients where the demographics are being presented on this subpopulation—of the total 3119 patients at baseline, we had removed 10 dead patients at discharge and removed 467 patients lost to follow-up; removed 53 patients with type of AF unknown. The definitions were investigator-categorized and were based on the ESC guidelines. Long-standing persistent is where there is a decision not to perform catheter ablation anymore and was intended to replace the cohort 'permanent' in ablation-focused reports.

*P-values for among-group comparisons are from Pearson's χ^2 test.

**P-values for among-group comparisons are from the Kruskal–Wallis test.

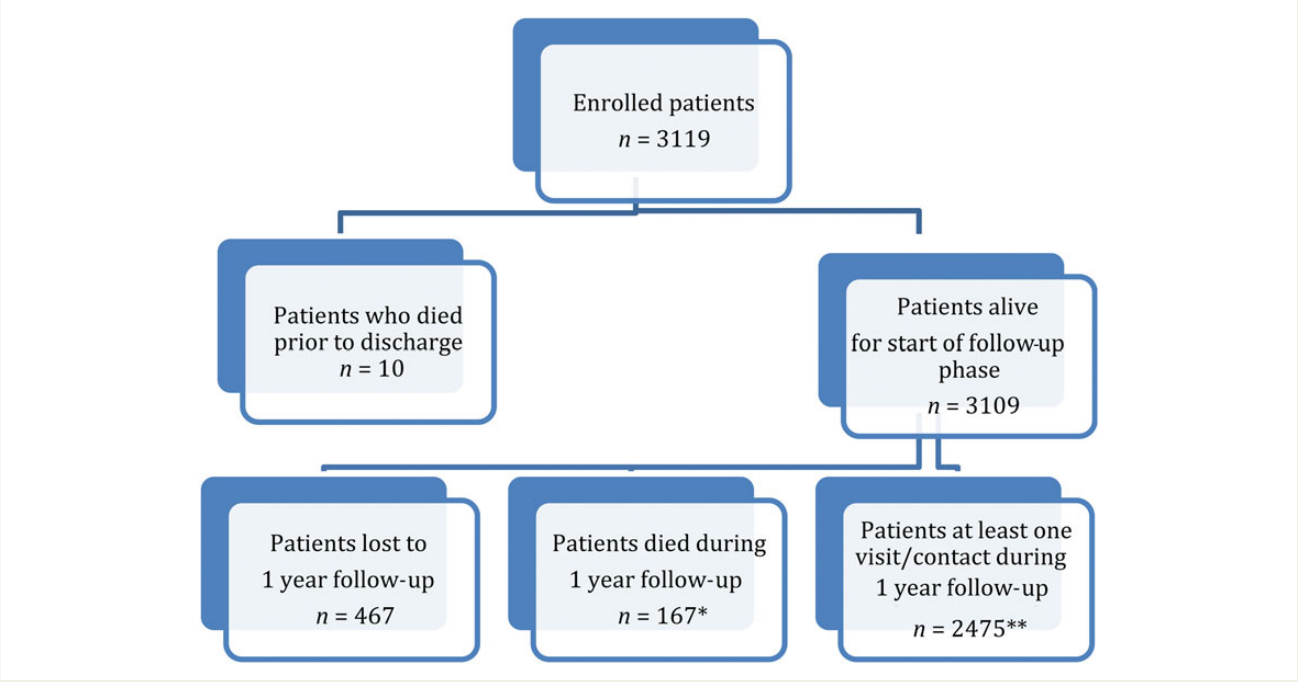

Figure 1 Patient flow as part of the EORP-AF pilot general registry. *1 Patient with type of atrial fibrillation unknown. **52 Patients with type of atrial fibrillation unknown.

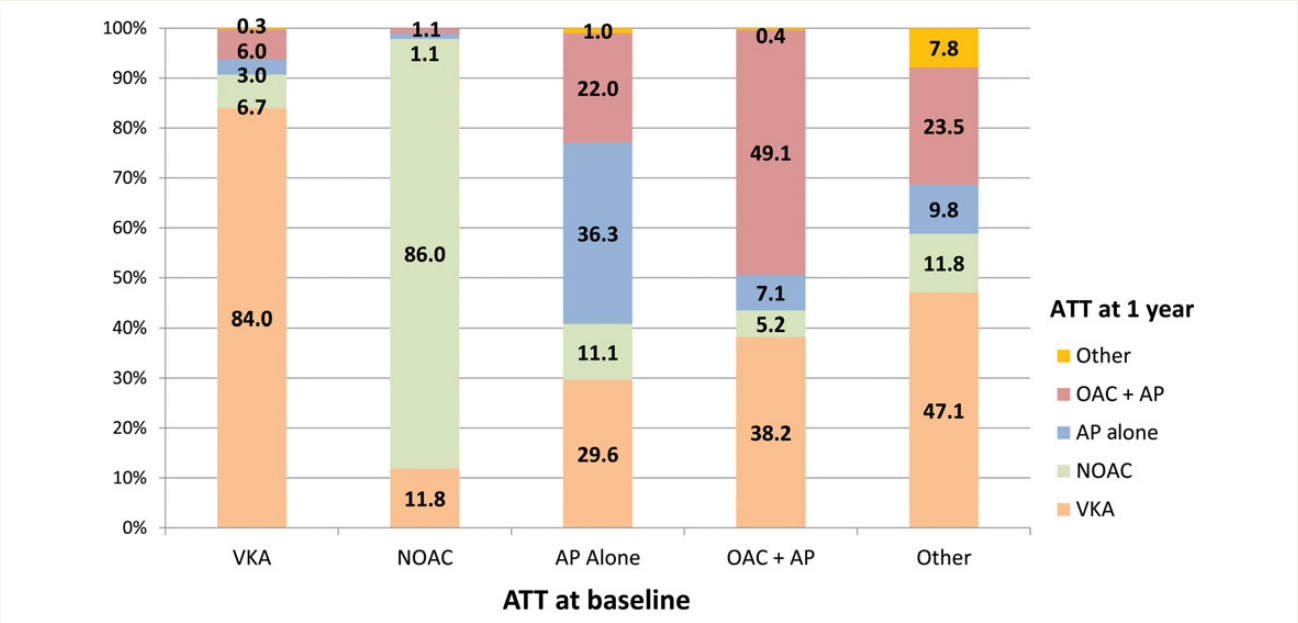

Figure 2 Antithrombotic therapy use at 1 year based on initial/baseline antithrombotic regimen. ATT, antithrombotic therapy; VKA, vitamin K antagonist; AP, antiplatelet therapy (most commonly aspirin); OAC, oral anticoagulant therapy.

multivariable model (logistic regression) to identify the independent predictors of all-cause death and/or stroke/transient ischaemic attack (TIA)/peripheral embolism during the 1-year follow-up period.

A two-sided *P*-value of <0.05 was considered as statistically significant. All analyses were performed using the SAS statistical software version 9.4 (SAS Institute, Inc., Cary, NC, USA).

Results

Patient demography in relation to clinical subtype of AF is summarized in *Table 1*. The patient disposition is shown in *Figure 1*, where of the 3109 patients who were enrolled and alive at baseline, 2475 (79.6%) had at least one visit/contact during the follow-up, while

Table 2 Drug therapies prescribed at follow-up

	Total	First detected	Paroxysmal	Persistent	Long-standing persistent AF	Permanent	*P*-value
(a) Antithrombotic drugs by AF subgroup							
Oral anticoagulation drug (at least one OAC) (%)							
Pre-follow-up consultation	78.5 (1903/2423)	70.4 (496/705)	76.5 (509/665)	86.0 (449/522)	78.9 (90/114)	86.1 (359/417)	<0.0001*
After follow-up consultation	77.5 (1877/2423)	68.7 (484/705)	76.2 (507/665)	83.9 (438/522)	78.1 (89/114)	86.1 (359/417)	<0.0001*
VKA (%)							
Pre-follow-up consultation	68.1 (1650/2423)	59.7 (421/705)	65.6 (436/665)	74.5 (389/522)	73.7 (84/114)	76.7 (320/417)	<0.0001*
After follow-up consultation	66.4 (1610/2423)	58.2 (410/705)	64.2 (427/665)	71.5 (373/522)	71.9 (82/114)	76.3 (318/417)	<0.0001*
NOAC (at least one NOAC) (%)							
Pre-follow-up consultation	10.5 (255/2423)	10.8 (76/705)	11.1 (74/665)	11.7 (61/522)	5.3 (6/114)	9.1 (38/417)	0.2591*
After follow-up consultation	11.0 (267/2423)	10.5 (74/705)	12.3 (82/665)	12.3 (64/522)	6.1 (7/114)	9.6 (40/417)	0.2132*
Antiplatelet drug (at least one AP) (%)							
Pre-follow-up consultation	29.0 (703/2423)	31.5 (222/705)	27.1 (180/665)	27.8 (145/522)	45.6 (52/114)	24.9 (104/417)	0.0002*
After follow-up consultation	27.6 (669/2423)	29.8 (210/705)	25.7 (171/665)	26.2 (137/522)	43.0 (49/114)	24.5 (102/417)	0.0008*

	Total	Low	Moderate	High	*P*-value
(b) Antithrombotic therapy by stroke risk strata					
Oral anticoagulation drug (at least one OAC) (%)					
Pre-follow-up consultation	78.7 (1947/2475)	50.0 (109/218)	74.2 (204/275)	82.4 (1634/1982)	<0.0001*
After follow-up consultation	77.7 (1923/2475)	50.5 (110/218)	72.7 (200/275)	81.4 (1613/1982)	<0.0001*
VKA (%)					
Pre-follow-up consultation	68.2 (1688/2475)	42.7 (93/218)	59.3 (163/275)	72.3 (1432/1982)	<0.0001*
After follow-up consultation	66.6 (1649/2475)	40.4 (88/218)	58.2 (160/275)	70.7 (1401/1982)	<0.0001*
NOAC (at least one NOAC) (%)					
Pre-follow-up consultation	10.5 (261/2475)	7.8 (17/218)	14.9 (41/275)	10.2 (203/1982)	0.0237*
After follow-up consultation	11.1 (274/2475)	10.1 (22/218)	14.5 (40/275)	10.7 (212/1982)	0.1446*
Antiplatelet drug (at least one AP) (%)					
Pre-follow-up consultation	28.9 (715/2475)	14.7 (32/218)	19.3 (53/275)	31.8 (630/1982)	<0.0001*
After follow-up consultation	27.5 (680/2475)	15.1 (33/218)	16.7 (46/275)	30.3 (601/1982)	<0.0001*

	Total	First detected	Paroxysmal	Persistent	Long-standing persistent AF	Permanent	*P*-value
(c) Rhythm/rate control drugs (at follow-up after consultation)							
Class Ia (quinidine) (%)	0.1 (2/2423)	0.1 (1/705)	0.0 (0/665)	0.2 (1/522)	0.0 (0/114)	0.0 (0/417)	0.8426*
Class Ic (flecainide or propafenone) (%)	9.3 (226/2423)	6.5 (46/705)	16.1 (107/665)	13.0 (68/522)	0.9 (1/114)	1.0 (4/417)	<0.0001*
Beta-blockers (%)	67.4 (1632/2423)	69.1 (487/705)	63.3 (421/665)	67.8 (354/522)	70.2 (80/114)	69.5 (290/417)	0.1220*
Class III (amiodarone or sotalol) (%)	22.7 (550/2423)	20.1 (142/705)	27.7 (184/665)	32.6 (170/522)	26.3 (30/114)	5.8 (24/417)	<0.0001*
Digitalis (mainly digoxin) (%)	49.0 (1188/2423)	49.8 (351/705)	35.8 (238/665)	49.6 (259/522)	63.2 (72/114)	64.3 (268/417)	<0.0001*

2.7% of patients at baseline were on no antithrombotic therapy.
P-values for among-group comparisons are from Pearson's χ^2 test.

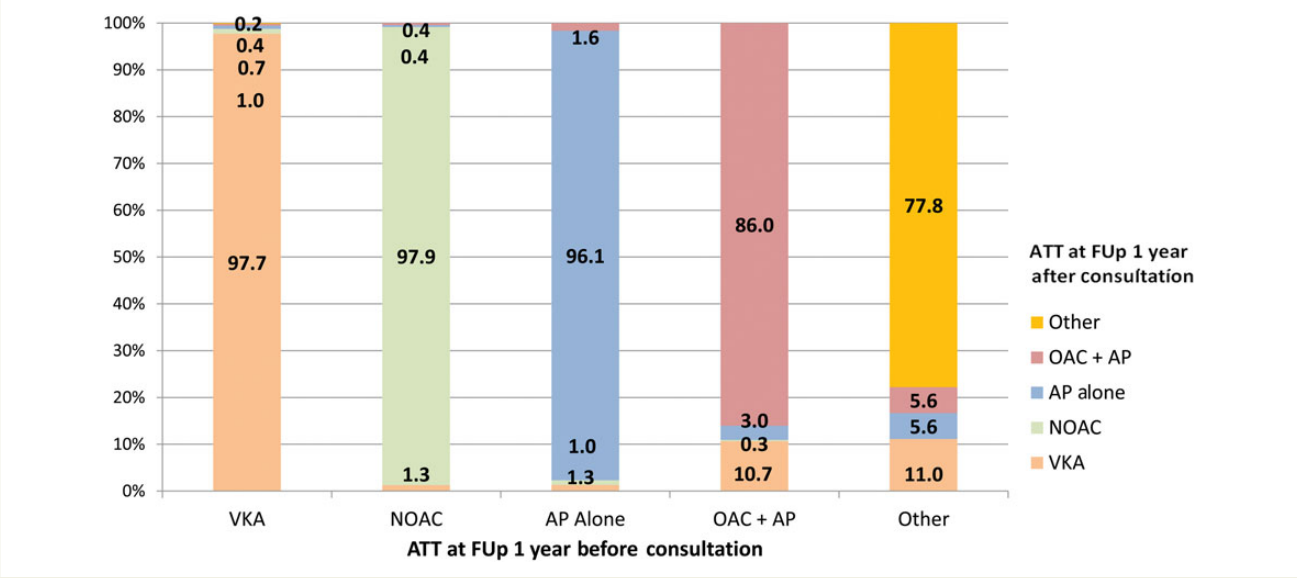

Figure 3 Antithrombotic therapy at 1 year comparing before vs. after visit/consultation. ATT, antithrombotic therapy; VKA, vitamin K antagonist; AP, antiplatelet therapy (most commonly aspirin); OAC, oral anticoagulant therapy.

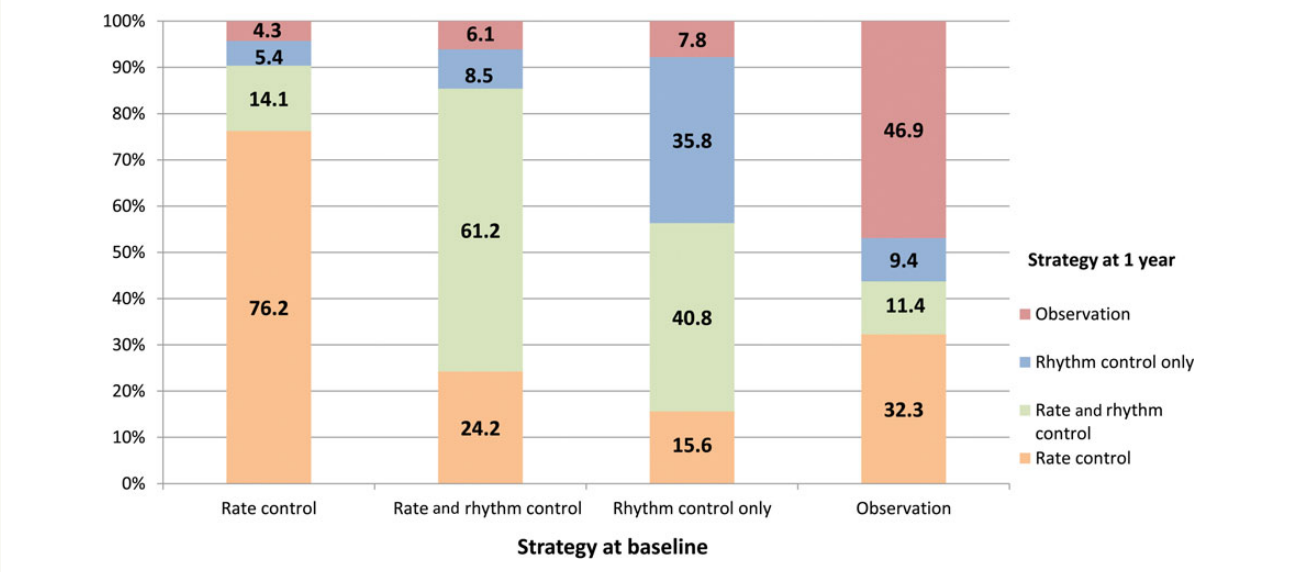

Figure 4 Rate or rhythm control strategies at 1 year in relation to baseline rhythm strategies.

167 (5.4%) died and 467 (15%) were lost to follow-up. The mean follow-up duration for the whole cohort was 366 days.

As expected, patients with permanent AF were older, although no statistically significant difference in a gender ratio was evident. Differences in stroke risk strata by the CHA_2DS_2-VASc score were similarly evident, with more high-risk patients in the permanent and long-standing persistent subgroups. This was also reflected in bleeding risk by HAS-BLED strata. More 'low-risk' patients presented with paroxysmal AF (*Table 1*).

Symptoms at follow-up

Of those patients with reported data, 23.2% were symptomatic at 1-year follow-up, most frequently among paroxysmal and persistent AF patients (24.8 and 27.8%, respectively). The most common symptoms at follow-up were palpitations (65.3%), fatigue (50.0%), and shortness of breath (43.1%); for palpitations, this was most frequent among paroxysmal and persistent AF patients (*Table 1*). Symptomatic status was not different in patients with low-, intermediate-, or high-stroke risk ($P = 0.4479$).

Table 3 Interventions performed by 1-year follow-up

	Total	First detected	Paroxysmal	Persistent	Long-standing persistent AF	Permanent	*P*-value
Pharmacological cardioversion (%)	5.1 (119/2344)	3.6 (25/692)	9.7 (63/647)	5.8 (28/485)	0.9 (1/111)	0.5 (2/409)	<0.0001*
Electrical cardioversion (%)	9.7 (232/2398)	8.0 (56/698)	11.1 (73/657)	16.7 (87/520)	9.7 (11/113)	1.2 (5/410)	<0.0001*
Catheter ablation (%)	4.4 (106/2405)	1.3 (9/700)	8.2 (54/661)	6.0 (31/520)	6.2 (7/113)	1.2 (5/411)	<0.0001*
Pacemaker implantation (%)	1.8 (44/2422)	1.3 (9/705)	2.3 (15/665)	2.5 (13/522)	0.0 (0/113)	1.7 (7/417)	0.2546*
Implantable defibrillator (%)	1.0 (24/2422)	1.1 (8/705)	0.8 (5/665)	0.8 (4/522)	0.9 (1/113)	1.4 (6/417)	0.7961*
AF surgery (%)	0.6 (14/2422)	0.4 (3/705)	0.9 (6/665)	0.8 (4/522)	0.9 (1/113)	0.0 (0/417)	0.2256*

ATT, antithrombotic therapy; VKA, vitamin K antagonist; AP, antiplatelet therapy (most commonly aspirin); OAC, oral anticoagulant therapy; NOAC, non-VKA oral anticoagulant.
*P-values for among-group comparisons are from Pearson's χ^2 test.

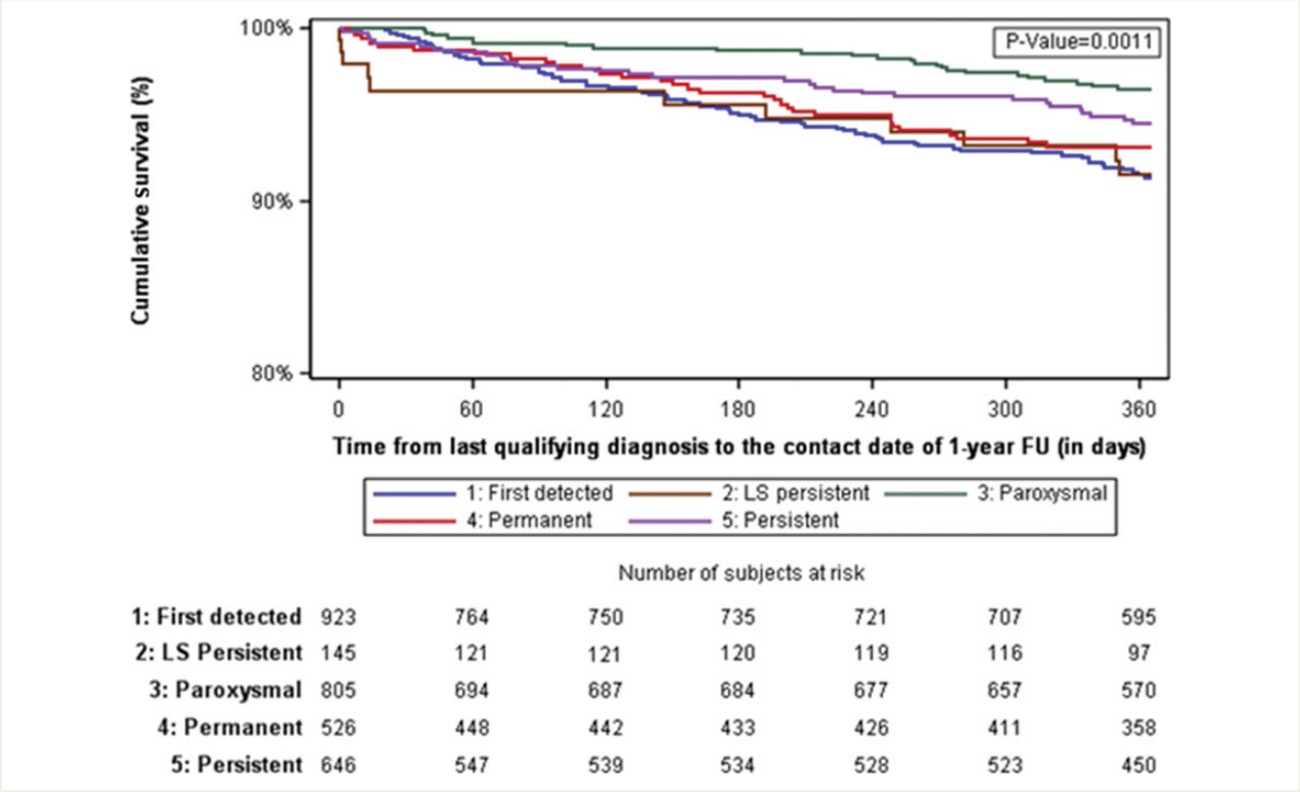

Figure 5 Kaplan–Meier curves for mortality in relation to atrial fibrillation subtype.

Antithrombotic therapy

Figure 2 shows antithrombotic therapy use at a 1-year follow-up visit, in relation to antithrombotic therapy used at the baseline registry entry visit. Of those on a vitamin K antagonist (VKA), 84% remained on VKA during the follow-up, while of those on non-VKA oral anticoagulant (NOAC) at baseline, 86% remained on NOAC, and 11.8% had changed to a VKA and 1.1% to antiplatelet therapy alone. Of those on antiplatelet therapy, 62% were on an oral anticoagulant (OAC; with 22% in combination with an antiplatelet).

Drug therapies prescribed at follow-up are shown in *Table 2*, summarising drugs used pre- and after- the follow-up consultation. Overall OAC use remains high, approximately 78% overall at follow-up, and proportions of VKA and NOAC remains broadly similar pre- and after- the follow-up consultation visit (*Table 2*, *Figure 3*). Oral anticoagulant use was the highest among persistent and permanent AF (84–86%), with NOACs relatively more common (but non-significant) among paroxysmal and persistent AF. Antiplatelet therapy was used in 29% at follow-up, more commonly among long-standing persistent AF.

Table 4 Mortality and morbidity during the follow-up

	Total	First detected	Paroxysmal	Persistent	Long-standing persistent AF	Permanent	*P*-value
(a) Mortality (all)							
Death (%)	5.8 (176/3049)	7.5 (69/923)	3.5 (28/808)	4.9 (32/647)	8.3 (12/145)	6.7 (35/526)	0.0029*
Causes of death (details) (%)							
Cardiac	57.4 (66/115)	51.0 (25/49)	50.0 (9/18)	58.8 (10/17)	55.6 (5/9)	77.3 (17/22)	0.0288*
Vascular	13.0 (15/115)	8.2 (4/49)	22.2 (4/18)	11.8 (2/17)	44.4 (4/9)	4.5 (1/22)	
Non-cardiovascular	29.6 (34/115)	40.8 (20/49)	27.8 (5/18)	29.4 (5/17)	0.0 (0/9)	18.2 (4/22)	
Cardiac (%)							
Acute myocardial infarction	7.6 (5/66)	0.0 (0/25)	11.1 (1/9)	20.0 (2/10)	40.0 (2/5)	0.0 (0/17)	0.0186*
Heart failure	77.3 (51/66)	84.0 (21/25)	77.8 (7/9)	50.0 (5/10)	40.0 (2/5)	94.1 (16/17)	
Arrhythmia	7.6 (5/66)	8.0 (2/25)	11.1 (1/9)	10.0 (1/10)	20.0 (1/5)	0.0 (0/17)	
Other	7.6 (5/66)	8.0 (2/25)	0.0 (0/9)	20.0 (2/10)	0.0 (0/5)	5.9 (1/17)	
Vascular (%)							
Ischaemic stroke	20.0 (3/15)	0.0 (0/4)	0.0 (0/4)	0.0 (0/2)	50.0 (2/4)	100.0 (1/1)	0.5684*
Haemorrhagic stroke	53.3 (8/15)	75.0 (3/4)	50.0 (2/4)	50.0 (1/2)	50.0 (2/4)	0.0 (0/1)	
Pulmonary embolism	20.0 (3/15)	25.0 (1/4)	25.0 (1/4)	50.0 (1/2)	0.0 (0/4)	0.0 (0/1)	
Aorto-oesophageal fistula	6.7 (1/15)	0.0 (0/4)	25.0 (1/4)	0.0 (0/2)	0.0 (0/4)	0.0 (0/1)	
(b) Readmissions							
Readmission for AF/atrial flutter/atrial tachycardia (%)	17.9 (400/2238)	12.8 (87/679)	21.9 (137/627)	28.7 (137/477)	23.3 (17/73)	5.8 (22/382)	<0.0001*
Readmission: other cardiovascular events (%)	11.7 (265/2258)	15.1 (104/689)	7.4 (47/631)	10.2 (48/470)	10.5 (8/76)	14.8 (58/392)	0.0001*
ACS (%)	7.2 (19/264)	4.8 (5/104)	21.3 (10/47)	4.2 (2/48)	0.0 (0/7)	3.4 (2/58)	0.0098*
Heart failure (%)	42.8 (113/264)	42.3 (44/104)	29.8 (14/47)	35.4 (17/48)	28.6 (2/7)	62.1 (36/58)	0.0083*
Coronary intervention (%)	20.1 (53/264)	21.2 (22/104)	34.0 (16/47)	18.8 (9/48)	14.3 (1/7)	8.6 (5/58)	0.0298*
Arrhythmia, other than AF/atrial flutter (%)	11.0 (29/264)	8.7 (9/104)	12.8 (6/47)	18.8 (9/48)	28.6 (2/7)	5.2 (3/58)	0.0950*
Cardiac arrest (%)	1.5 (4/264)	2.9 (3/104)	0.0 (0/47)	2.1 (1/48)	0.0 (0/7)	0.0 (0/58)	0.6171*
Stroke (%)	5.7 (15/264)	6.7 (7/104)	4.3 (2/47)	4.2 (2/48)	0.0 (0/7)	6.9 (4/58)	0.9450*
TIA (%)	2.3 (6/264)	0.0 (0/104)	4.3 (2/47)	4.2 (2/48)	14.3 (1/7)	1.7 (1/58)	0.0277*
Peripheral embolism (%)	1.1 (3/263)	1.0 (1/104)	0.0 (0/46)	0.0 (0/48)	0.0 (0/7)	3.4 (2/58)	0.4025*
Non-cardiovascular events (%)	12.6 (286/2261)	13.3 (90/678)	12.8 (81/635)	11.1 (52/467)	8.1 (7/86)	14.2 (56/395)	0.4579*
Bleeding (%)	8.4 (24/286)	11.1 (10/90)	2.5 (2/81)	9.6 (5/52)	14.3 (1/7)	10.7 (6/56)	0.1304*

ACS, acute coronary syndrome; TIA, transient ischaemic attack.
*P-values for among-group comparisons are from Pearson's χ^2 test.

Antithrombotic therapy use by stroke risk strata (based on the CHA_2DS_2-VASc score) is shown in *Table 2B*. Oral anticoagulant was used in 50% of low-risk patients, of whom 35.2% (76/216) were planned for cardioversion and/or ablation procedures. Otherwise OAC was used in 73–74% of moderate risk (CHA_2DS_2-VASc score = 1 in males) and ~81–82% of high-risk (CHA_2DS_2-VASc score ≥2) patients. Vitamin K antagonist was the most commonly used OAC, especially among high-risk patients. Non-VKA oral anticoagulants were commonly used in moderate-risk patients (~15%). Antiplatelet therapy (commonly aspirin) was used in 15% of low-risk, and 31% of high-risk patients.

Rate and rhythm control drugs

Rhythm/rate control drugs used at follow-up are summarized in *Table 2C*. Beta-blockers and digitalis remained the most common drugs used, especially among permanent and long-standing persistent AF patients. Class Ic and III drugs were commonly used in paroxysmal and persistent AF. Digoxin was used in 35.8% of paroxysmal AF patients. Those patients planned for rate control at baseline were continued in a rate control strategy in 76%, while rhythm control was considered in 19.5% (*Figure 4*). Of those considered for a rhythm control management strategy at baseline, 15.6% were now being considered for a rate control strategy.

Of the interventions performed by the 1-year follow-up, electrical, and pharmacological cardioversion had been performed in 9.7 and 5.1%, respectively—especially among paroxysmal or persistent AF patients. Catheter ablation had been performed in 4.4%, particularly among paroxysmal or persistent (and long-standing persistent) AF patients (*Table 3*).

Mortality and morbidity

After 1 year, 5.7% (177/3119) of the patients enrolled in the study died between the time of enrolment and the 1-year follow-up visit. The highest mortality rates were in the first detected (7.5%) and in the long-standing persistent AF (8.3%) groups.

Kaplan–Meier curves for mortality between known AF subgroups are shown in *Figure 5*. Causes were cardiac (57.4%; 66/115), vascular (13.0%; 15/115), and non-cardiovascular (29.6%; 34/115), with no significant differences between AF subgroups—, cardiac causes were more common in permanent AF patients and vascular causes were more common in long-standing persistent AF patients. Of the 66 cardiac deaths, heart failure (77.3%) was the most common cause of death [*Table 4(a)*]. Of the 15 vascular deaths, stroke was the cause of 11 deaths (3 ischaemic, 8 haemorrhagic), pulmonary embolism caused 3 deaths, and aorto-oesophageal fistula in 1 case. No pro-arrhythmic deaths were evident.

There were no cardiovascular deaths among 'low-risk' patients at 1 year. There were no ischaemic strokes but one case of haemorrhagic stroke in a 'moderate-risk' patient that resulted in death. Stroke/TIA/peripheral embolism occurred in 1 case (which was a TIA) among 'low-risk' patients, and one case among 'moderate-risk' patients.

Of those 2475 patients completing the 1-year follow-up visit, there were 411 readmissions for AF/atrial flutter, 290 readmissions for non-cardiovascular events (including 25 hospital admissions for bleeding) and 271 readmissions for other cardiovascular events. In this latter population, there were 15 strokes, 7 TIAs, 3 peripheral embolism, and 116 hospital admissions for heart failure [*Table 4(b)*]. New onset diabetes was diagnosed in 1.2%, peripheral vascular disease in 0.8%, and renovascular disease in 0.7%.

Multivariate analysis

On a stepwise model, multivariate predictors of stroke/TIA/peripheral embolism and/or mortality are shown in *Table 5* and *Figure 6*.

For stroke/TIA/peripheral embolism and/or mortality, independent predictors were age (OR: 1.06, $P < 0.0001$), AF as primary presentation (OR: 2.44, $P < 0.0001$), previous TIA (OR: 2.37, $P = 0.0033$), chronic kidney disease (OR: 2.69, $P < 0.0001$), chronic heart failure (OR: 2.05, $P = 0.0001$), malignancy (OR: 1.77, $P = 0.0467$) and minor bleeding (OR: 1.97, $P = 0.0141$).

For mortality, independent predictors were age (OR: 1.06, $P < 0.0001$), chronic kidney disease (OR: 3.33, $P < 0.0001$), chronic obstructive pulmonary disease (OR: 1.65, $P = 0.0241$), malignancy (OR: 1.82, $P = 0.0474$), minor bleeding (OR: 2.25, $P = 0.0044$), AF as primary presentation (OR: 2.72, $P < 0.0001$), prior TIA (OR: 2.37, $P = 0.0048$), and diuretic use (OR: 1.71, $P = 0.0119$). Statin use was predictive of lower mortality (OR: 0.65, $P = 0.0153$).

Discussion

In this 1-year follow-up analysis of the EORP-AF pilot general registry, our principal findings are as follows: (i) patients are frequently

Table 5 Multivariate analysis

Clinical variable	Odds ratio estimates			
	Point estimate	95% CI		*P*-value
(a) Stroke/TIA/peripheral embolism and/or mortality				
Age	1.063	1.043	1.081	<0.0001
AF as primary reason for admission/ consultation	2.439	1.600	3.353	<0.0001
Chronic heart failure	2.046	1.377	2.890	0.0001
Previous TIA	2.366	1.392	4.395	0.0033
Chronic kidney disease	2.690	1.947	3.965	<0.0001
Malignancy	1.770	1.008	3.107	0.0467
Bleeding	1.965	1.146	3.368	0.0141
(b) Mortality				
Age	1.060	1.040	1.081	<0.0001
AF as reason for admission/ consultation	2.716	1.820	4.055	<0.0001
Previous TIA	2.371	1.301	4.321	0.0048
Chronic kidney disease	3.325	2.293	4.822	<0.0001
Chronic obstructive pulmonary disease	1.647	1.068	2.541	0.0241
Malignancy	1.816	1.007	3.276	0.0474
Bleeding	2.248	1.287	3.929	0.0044
Diuretics	1.712	1.126	2.604	0.0119
Statins	0.645	0.452	0.919	0.0153

AF, atrial fibrillation; TIA, transient ischaemic attack.

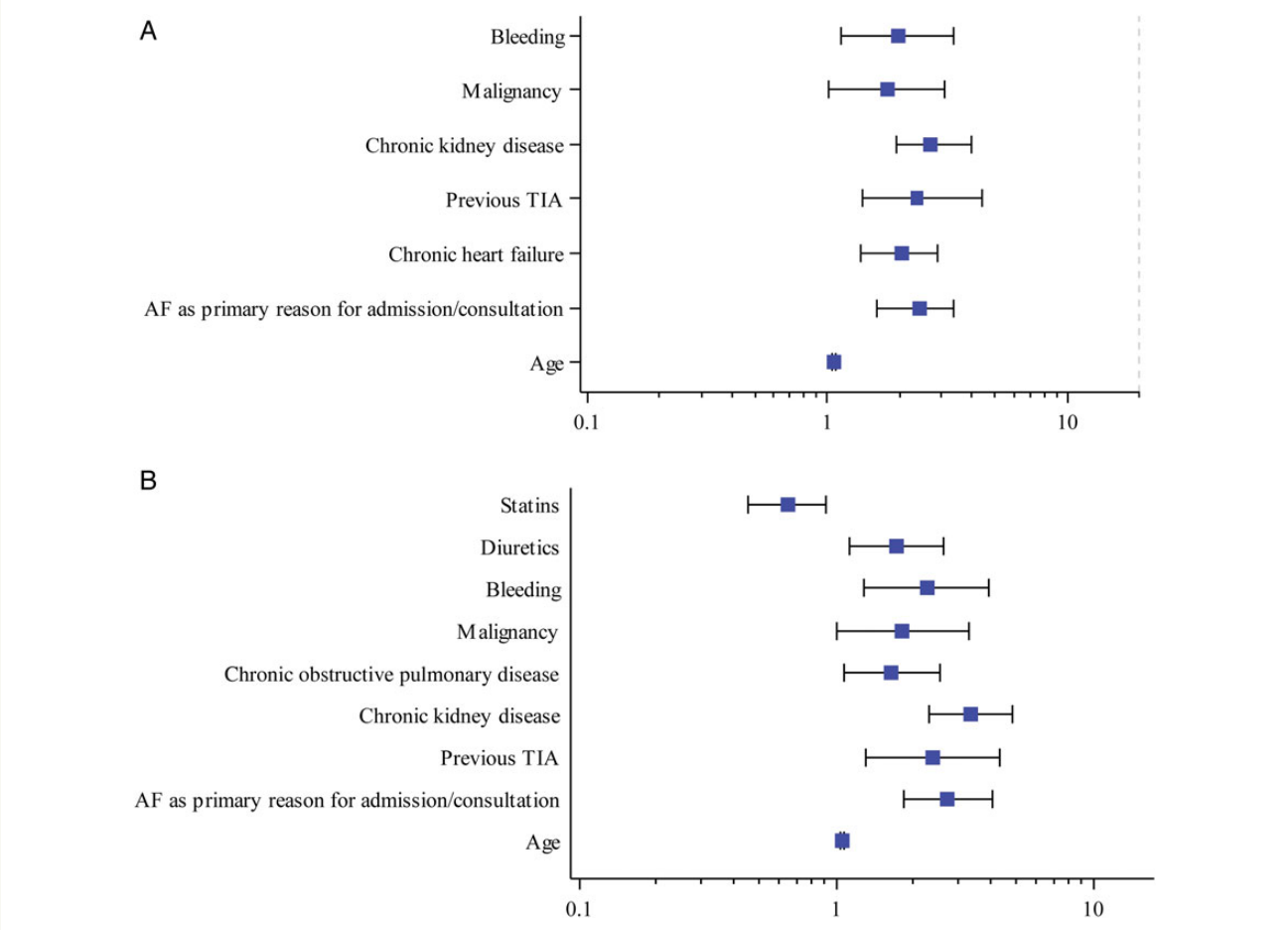

Figure 6 Forest plots showing odds ratios (and 95% CIs) for multivariate predictors of stroke/transient ischaemic attack/peripheral embolism and/or mortality. (*A*) Stroke/transient ischaemic attack/peripheral embolism and/or mortality. (*B*) All-cause mortality.

asymptomatic but symptoms are nevertheless still common among some AF patients, especially palpitations, fatigue, and shortness of breath; (ii) overall OAC use remains high, and at 1-year follow-up, >84% remained on anticoagulation, with an minority changing type of antithrombotic therapy; (iii) rhythm control was infrequent, with cardioversion being performed in ~15% of patients and catheter ablation in only 4.4%, (iv) 1-year mortality was high in AF patients (6.4%), with 70% being cardiovascular deaths, but those classed at low risk using the CHA_2DS_2-VASc score had low mortality and no stroke/peripheral embolism events; and (v) hospital readmissions were common, especially for AF and heart failure.

This survey represents the first contemporary registry focused on management practices among European cardiologists, with associated follow-up data, conducted since the publication of the new ESC guidelines in 2010[7] and its focused update in 2012.[1] While other general AF management surveys have been published or presented (most of which are conducted and sponsored by industry, many of which are also larger and includes patients looked after by cardiologists and non-cardiologists[10–13]), our focus was a well-conducted contemporary ESC-conducted survey on clinical practice and follow-up among European cardiologists.

While patients are frequently asymptomatic overall, symptoms at 1-year follow-up are nevertheless common among paroxysmal and persistent AF patients, particularly palpitations.[14] The management of AF has become more patient centred and symptom directed,[15] and decisions on rate or rhythm control have focused on symptomatic status. This is reflected by a very limited use of antiarrhythmic drugs, cardioversions, and catheter ablations in (usually symptomatic) patients, and the low rate of rhythm control interventions in the present study. Indeed, rate control drugs were often used even in paroxysmal or persistent AF patients for symptoms (as recommended in recent guidelines[16]), despite some evidence that digoxin may potentially make paroxysmal AF worse.[17]

Stroke prevention is central to AF management. Overall OAC use was much higher in the EORP-AF survey compared with the Euro-Heart survey on AF conducted a decade ago,[18] being prescribed in ~75% overall at follow-up. The 1-year follow-up data shows that persistence on VKA was 84%, while those on NOAC at baseline, 86% remained on the drug. This is important since suboptimal adherence and compliance with NOACs has important implications for stroke prevention management, being associated with a significant increase in stroke and death.[19,20] Despite the recommendations in guidelines,

we found that antiplatelet therapy (commonly aspirin) was still used in 15% of low risk, and in 31% of high-risk patients. When VKA or NOAC was discontinued, a small minority was started on antiplatelet therapy, although there is little evidence that aspirin is any safer than OACs.

Our data confirm the high mortality and morbidity associated with AF, even in contemporary clinical practice among European cardiologists. Indeed, 1-year mortality was high in AF patients (5.7%), particularly from heart failure, which is consistent with other cohort studies. As expected, independent predictors for stroke/TIA/peripheral embolism and/or mortality included clinical risk factors such as previous TIA, chronic kidney disease, and chronic heart failure. This is consistent with the high risks associated with such comorbidities in AF patients.[21,22] While diuretics increased mortality in our cohort, this may be related to disease severity (especially heart failure) or perhaps interactions(s) with antiarrhythmic drugs (especially with electrolyte abnormalities e.g. hypokalaemia). Interestingly, statins were protective against mortality in AF patients, consistent with other observations in AF patients.[23] This may reflect the high cardiovascular burden associated with AF, and statins have an important impact on adverse cardiovascular outcomes in general.[24]

The burden of hospitalizations associated with AF is increasingly recognized as a major healthcare cost, especially given the increasingly elderly population and greater prevalence of AF.[25] Indeed, hospital re-admissions were common in our cohort, especially for atrial tachyarrhythmias and heart failure. Hospitalizations *per se* also carry an adverse prognosis, increasing the risk of mortality in AF patients.[26] Of note, those classed at low risk using the CHA_2DS_2-VASc score had low mortality and no stroke/peripheral embolism events, consistent with prior studies in AF and non-AF populations,[27–31] demonstrating that the CHA_2DS_2-VASc score can also reliably predict the risk of all-cause death and not only of ischemic stroke.

Limitations

This study is limited by its observational registry design, but we have tried to overcome this by recruitment of consecutive patients in contemporary clinical practice reflecting the country-specified patterns. The participating countries are also from Europe, a relatively affluent part of the world, compared with some developing countries, where management differences are evident.[32] The patients were all seen by cardiologists (whereas other registries included all-comers collected by internists, neurologists, and general practitioners), which may partly explain the high 1-year event rates. Our proportion lost to follow-up (15%) is also a limitation but is much less than the figure seen in the original EuroHeart survey conducted a decade ago.

For our VKA-treated patients, we did not have information on quality of INR control, as reflected by time in therapeutic range (TTR), given the strong relationship to better outcomes with good anticoagulation control.[33,34] Finally, residual confounding is likely, given the 'real-world' observational design and non-randomized nature of some drug therapies with the possibility of confounding by indication. The relatively low reported numbers undergoing ablation or device implantation, as well as antiarrhythmic drug use, are additional limitations that preclude detailed analyses of the impact of these interventions in the present 'general' registry.

Conclusion

In this 1-year follow-up analysis of the EORP-F pilot general registry, we provide data on the first contemporary registry focused on management practices among European cardiologists, with associated follow-up data, conducted since the publication of the new ESC guidelines. Overall OAC use remains high, although persistence with therapy may be problematic. Nonetheless, continued OAC use was more common than in prior reports. Despite the high prescription of OAC, 1-year mortality and morbidity remain high in AF patients, particularly from heart failure and re-hospitalizations.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

Acknowledgements

The full list of EORP-AF investigators are provided in the Supplementary material online, *Appendix*. Competing interests are also provided.

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