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Age-Related Differences in Presentation, Treatment, and Outcome of Patients With Atrial Fibrillation in Europe

The EORP-AF General Pilot Registry (EURObservational Research Programme-Atrial Fibrillation)

Stefano Fumagalli, MD, PhD,* Salah A.M. Said, MD, PhD,† Cecile Laroche, MSc,‡ Debbie Gabbai, MD,* Niccolò Marchionni, MD,* Giuseppe Boriani, MD, PhD,§ Aldo P. Maggioni, MD,‡ Mircea Ioachim Popescu, MD, PhD,‖ Lars Hvilsted Rasmussen, MD, PhD,¶ Harry J.G.M. Crijns, MD,# Gregory Y.H. Lip, MD,**
on behalf of the EORP-AF Investigators

ABSTRACT

OBJECTIVES This study sought to compare age-related differences in presentation, treatment, and outcome of atrial fibrillation (AF) in a wide cohort of European subjects.

BACKGROUND AF is the most common sustained arrhythmia in the elderly.

METHODS We evaluated all patients enrolled in the EORP-AF (EURObservational Research Programme-Atrial Fibrillation) General Pilot Registry in 70 centers of 9 European countries.

RESULTS Among 3,119 subjects, 1,051 (33.7%) were age ≥75 years. Permanent AF was significantly more common in the elderly, who had a higher prevalence of hypertension, valvular diseases, chronic heart failure, coronary artery disease, renal failure, chronic obstructive pulmonary disease, and prior hemorrhagic event or a transient ischemic attack. Common diagnostic tests were underused in older subjects. Despite their higher stroke risk, the use of oral anticoagulants was significantly lower in the elderly (76.7% vs. 82.8%; $p = 0.0012$), whereas aspirin and clopidogrel alone or in combination were more often prescribed. Rate control was the management of choice in the older group, with electrical cardioversion and catheter ablation performed less frequently than in the younger age group. Antiarrhythmic drugs were significantly less prescribed in the elderly (29.8% vs. 41.7%; $p < 0.0001$). At the 1-year follow-up, mortality (11.5% vs. 3.7%; $p < 0.0001$) and the composite of stroke/transient ischemic attack, systemic thromboembolism, and/or death (13.6% vs. 4.9%; $p < 0.0001$) were significantly higher in the ≥75 years of age cohort.

CONCLUSIONS In older patients, AF is more often associated with comorbidities. Rate control is the preferred therapeutic approach. Despite a higher CHA_2DS_2-VASc score, the use of oral anticoagulation is suboptimal. In elderly subjects, the rate of adverse events is higher at follow-up. (J Am Coll Cardiol EP 2015;1:326–34)

From the *Division of Geriatric Cardiology and Medicine, Department of Experimental and Clinical Medicine, University of Florence and AOU Careggi, Florence, Italy; †Department of Cardiology, Hospital Group Twente, Almelo-Hengelo, Hengelo, the Netherlands; ‡EURObservational Research Programme Department, European Society of Cardiology, Sophia Antipolis, France; §Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, S. Orsola Malpighi University Hospital, Bologna, Italy; ‖County Emergency Hospital, Oradea, Romania; ¶Aalborg University Hospital, Aalborg, Denmark; #Department of Cardiology, Maastricht University Medical Center, Maastricht, the Netherlands; and the **University of Birmingham, Center for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom. At the time of the registry, the following companies were supporting the EURObservational Research Programme: Abbott Vascular International, Amgen, Bayer Pharma AG, Boston Scientific International, The Bristol-Myers Squibb and Pfizer Alliance, Boehringer Ingelheim, The Alliance Daiichi Sankyo Europe GmbH and Eli Lilly and Company, Menarini International Operations, Merck & Co. International, Novartis Pharma, Sanofi-Aventis Group, and SERVIER. Dr. Fumagalli held lectures for BMS/Pfizer; and was an investigator for a study sponsored by A. Menarini Industrie Farmaceutiche Riunite. Dr. Boriani received a small speakers fee (less than €1,200) from Boehringer, Medtronic Inc.,

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, with a prevalence and incidence that increase with age (1-3). From 2010 to 2060, the number of subjects age ≥55 years with AF in the European Union is expected to more than double, resulting in a rise of affected population from 8.8 to 17.9 million (4). This is consistent with projections for the United States, where 5.6 million subjects (age >80 years in more than 50% of cases) are expected to present AF in 2050 (5).

The importance of AF in older patients goes beyond its epidemiological impact, being closely linked with increased mortality (6,7) and a higher burden of comorbidities that are common in advanced age, such as stroke (8), chronic heart failure (CHF) (9), and dementia (10).

It is therefore important to evaluate how AF is managed at older ages. Despite observational studies (5,11) and trials (12) that have proven that benefits from oral anticoagulants (OA) extend to the oldest segments of AF population, real world data consistently show that prescription rate of OA is inversely related to age.

The EHS-AF (Euro Heart Survey on Atrial Fibrillation) is an observational study performed by the European Society of Cardiology (ESC) between 2003 and 2004 (13), showing that older patients with AF were less often referred to a cardiologist and less adequately studied and treated (14). Even when OA are prescribed, advanced age is an independent predictor of reduced adherence (15) or premature interruption (16). An increased awareness of the importance of OA in the elderly (17), and an update of the ESC AF guidelines specifically addressing the management of OA with inclusion of newest non-vitamin K antagonist OA (NOACs) (18), are the main changes that have occurred after the EHS-AF study, which dates back more than 10 years (13).

Thus, ESC member countries deemed it was necessary to update the information on management of AF in Europe. The EORP-AF (EURObservational Research Programme-Atrial Fibrillation) General Pilot Registry was designed with this purpose (19), and the present analysis specifically addresses the age-related differences in presentation, treatment, and outcomes of patients with AF in that registry.

METHODS

The baseline features and main results from the EORP-AF Registry have been previously published (19). In brief, the Registry population comprised consecutive inpatients and outpatients with AF evaluated in 70 centers from 9 participating ESC countries. Subjects were screened for eligibility at the time of their presentation to a cardiologist and were enrolled only after electrocardiogram (ECG) documentation of AF by 12-lead ECG, 24-h Holter ECG, or other ECG recording. The qualifying episode of AF should have occurred within the last year, independently of its presence at the time of enrollment. A primary or secondary diagnosis of AF was allowed. Each center had to recruit a minimum of 20 consecutive patients, with a total target Registry population of 3,000 subjects. The enrollment phase started in February 2012 and was completed in March 2013. Three further follow-up visits were scheduled on a yearly basis. The protocol of the study was approved by the ethics committee of each center. All patients provided written informed consent.

HEALTH-RELATED QUALITY OF LIFE QUESTIONNAIRE. Health-related quality of life was assessed with a self-administered AF-specific questionnaire (AF-QoL), consisting of 18 items that explore 3 domains of psychological (7 items), physical (8 items), and sexual (3 items) activities. All questions refer to feelings perceived in the preceding month and can be answered on a 5-point Likert scale (from 1, "totally agree," to 5, "totally disagree"), with lower scores indicating greater negative impact of AF on health-related quality of life (20).

STATISTICAL ANALYSIS. In this subanalysis, patients were stratified into ≥75 years of age ("elderly") and <75 years ("reference") age groups. Continuous and categorical variables were reported as mean ± SD or as median (interquartile range), and as absolute values and related percentages, respectively. Between-group differences were tested with Kruskall-Wallis test and with chi-square test (or

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation
CAD = coronary artery disease
CHF = chronic heart failure
CI = confidence interval
CKD = chronic kidney disease
COPD = chronic obstructive pulmonary disease
ECG = electrocardiogram
ESC = European Society of Cardiology
NOACs = non-vitamin K antagonist oral anticoagulants
OA = oral anticoagulants
OR = odds ratio
TIA = transient ischemic attack

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TABLE 1 Clinical Characteristics of Patients by Age Group

	Whole Cohort (n = 3,119)	Age <75 yrs (n = 2,068)	Age ≥75 yrs (n = 1,051)	p Value
Age, yrs	69 ± 11	63 ± 9	81 ± 5	–
Male, %	59.6	64.8	49.4	<0.0001
Type of AF, %				
First detected	30.3	29.6	31.6	<0.0001
Paroxysmal	26.5	29.4	20.9	
Persistent	21.2	23.0	17.8	
Long-standing persistent	4.8	4.5	5.3	
Permanent	17.3	13.6	24.5	
AF as main diagnosis, %	60.2	66.2	48.2	<0.0001
Comorbidities, %				
Chronic heart failure	47.5	43.4	55.0	<0.0001
Systolic dysfunction				
Severe (EF <30%)	7.1	7.7	6.0	0.0066
Moderate (EF 30%–44%)	16.5	15.7	18.2	
Mild (EF 45%–54%)	21.1	19.6	24.1	
Normal (EF >55%)	55.3	57.1	51.6	
HFPEF	48.1	43.5	55.2	0.0002
Chronic kidney disease	13.1	9.0	21.3	<0.0001
COPD	11.0	8.7	15.5	<0.0001
Coronary artery disease	36.4	31.0	46.5	<0.0001
Diabetes mellitus	20.6	19.7	22.2	0.1058
Hemorrhagic event	5.9	4.8	8.0	0.0004
Hypertension	70.7	67.2	77.5	<0.0001
Hyperthyroidism	3.0	3.3	2.4	0.1697
Previous stroke	6.3	5.8	7.3	0.1082
Previous TIA	4.1	3.2	5.9	0.0003
Valvular heart disease	63.4	58.2	73.2	<0.0001
$CHADS_2$ score				
0	12.6	18.8	0.3	<0.0001
1	27.1	36.7	8.4	
≥2	60.3	44.5	91.3	
CHA_2DS_2-VASc score*				
Low risk	8.0	12.1	0.0	<0.0001
Moderate risk	10.3	15.4	0.1	
High risk	81.7	72.4	99.9	
HAS-BLED score				
0	21.7	32.7	0	<0.0001
1	37.7	37.5	38.1	
2	26.6	20.9	38.0	
≥3	14.0	9.0	24.0	

Continued on the next page

Fisher exact test when cell count was <5) for continuous and categorical variables, respectively.

A multivariable logistic regression model, including all significant univariable associations and those variables considered of relevant clinical interest (on the whole, "candidate variables"), was used to identify the predictors of antithrombotic therapy prescription. The search of the best predictive model was performed using the program R and the "glmulti" package, based on the Akaike Information Criterion, with the search option set to genetic algorithm. The following candidate variables were tested: prosthetic mechanical valve, hyperthyroidism, hypothyroidism, peripheral vascular disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), malignancy, liver disease, sleep apnea, hemorrhagic events, thromboembolic ischemic complications, age, body mass index, heart rate, systolic and diastolic blood pressure, and CHA_2DS_2-VASc and HAS-BLED scores. Two further multivariable logistic regression models were used to identify the independent predictors of all-cause mortality and of the composite of death, stroke/transient ischemic attack (TIA), and/or peripheral embolism at 1-year follow-up. In these cases, all database variables associated with the outcome variables at univariable analysis were entered in the final model. Two-sided $p < 0.05$ was considered statistically significant.

RESULTS

Of the 3,119 patients enrolled in the EORP-AF Registry, 33.7% (n = 1,051; mean age, 81 ± 5 years; 50.6% females) were ≥75 years of age. Compared with reference patients, elderly subjects had more frequently (47.5% vs. 41.1%; $p < 0.0001$) non-self-terminating forms of AF (persistent, long-standing persistent, or permanent AF), and among the several comorbidities explored, a higher prevalence of coronary artery disease (CAD), CKD, COPD, hypertension, previous hemorrhagic events, TIA, and valvular heart diseases (Table 1).

Despite similar mean heart rate and left ventricular ejection fraction (Table 1), CHF also was more common in the elderly. In older patients, systolic dysfunction, if present, was more often mild-to-moderate ($p < 0.0001$), with a higher prevalence of CHF with preserved ejection fraction (Table 1).

High stroke and bleeding risk were more common among the elderly, as indicated by higher prevalence of $CHADS_2$ or CHA_2DS_2-VASc score ≥2 and of HAS-BLED score ≥3 (Table 1).

SYMPTOMS AND HEALTH STATUS. Elderly patients were more frequently in European Heart Rhythm Association class I ($p < 0.001$) and were less often symptomatic (52.4% vs. 64.4%; $p < 0.0001$), with lower prevalence of palpitations and feelings of fear/anxiety partially counterbalanced by more frequent dyspnea (Table 1). At AF-QoL questionnaire, the total and physical domain scores were lower in the age ≥75 years group, with similar psychological and sexual activity domains scores.

DIAGNOSTIC PROCEDURES AND TREATMENT STRATEGY. Transthoracic echocardiography, ECG Holter monitoring, and exercise testing were used significantly less in the elderly subgroup (Table 2).

A rate-control strategy was more frequently adopted in the elderly, with lower proportions of electrical cardioversion, transcatheter ablation (Table 2), and prescription of antiarrhythmic drugs (Table 3). Only pacemaker implantation was more common in the elderly (Table 2). Among rate-control agents, beta-blockers were similarly prevalent in both groups, whereas digoxin and nondihydropyridine calcium-channel blockers were more often prescribed to older patients (Table 3). Diuretics, statins, and aldosterone blockers were also more frequently used in the elderly (Table 3).

OA were prescribed less frequently in older patients (Table 3), who more frequently received aspirin or clopidogrel, either alone or in combination (Table 3). In keeping with more prevalent CAD, older patients more often used the combination of OA with single or double antiplatelet therapy (28.9% vs. 22.8%; p = 0.0032).

MULTIVARIABLE ANALYSES. At multivariable analysis, prescription of OA in the elderly group was reduced by 69% and 46% for each year of increasing age and in the presence of CKD, respectively (Figure 1), whereas no significant predictor was found in the younger group. Further multivariable models showed that prescription of antiplatelet drugs was negatively associated with female sex, CKD, and a history of hemorrhagic events, and positively associated with HAS-BLED score in both age cohorts, whereas a negative association with hyperthyroidism was found only in the older group (Figure 1).

EVENTS IN-HOSPITAL AND IN THE 2 WEEKS AFTER DISCHARGE OR CONSULTATION. During hospitalization or in the 2 weeks after discharge from hospital or consultation, older patients had a higher incidence of minor bleeding (1.24% vs. 0.48%; p = 0.0201) and of asystole (0.86% vs. 0.29%; p = 0.0307). No difference was observed in major bleedings, cardioembolic events, new episodes of CHF, AF relapse, or occurrence of major ventricular arrhythmias. In-hospital mortality did not differ between older (n = 6 of 653; 0.9%) and younger patients (n = 4 of 1,366; 0.3%) (p = 0.0863).

1-YEAR OUTCOMES. Overall, 2,642 subjects (84.7%) underwent the scheduled 1-year visit, with a mean follow-up of 366 ± 32 days. Mortality and the composite of stroke-TIA, systemic thromboembolism, and death were higher in patients ≥75 years of age (11.5% vs. 3.7%, odds ratio [OR]: 3.33, 95% confidence interval [CI]: 2.41 to 4.59; 13.6% vs. 4.9%, OR: 3.08, 95% CI: 2.28 to 4.17; p < 0.0001 for both). At multivariable logistic regression analysis (Table 4), age ≥75 years, AF not representing the main reason for hospitalization/evaluation, a history of CKD, COPD, malignancy, minor bleeding and/or TIA, and use of diuretics or oral antidiabetic agents were independent predictors of mortality. Statin therapy was associated with lower mortality rates. Analysis adjustment for either country of enrollment or for significant interaction terms did not modify these results. After introducing CHF into and removing COPD and oral antidiabetics from the model, the same variables associated with mortality predicted also the composite endpoint.

TABLE 1 Continued

	Whole Cohort (n = 3,119)	Age <75 yrs (n = 2,068)	Age ≥75 yrs (n = 1,051)	p Value
EHRA score, %				
Class I	39.7	35.6	47.6	<0.0001
Class II	30.9	35.0	22.8	
Class III	23.9	24.1	23.6	
Class IV	5.5	5.3	6.0	
Currently symptomatic, %	60.3	64.4	52.4	<0.0001
Nonsymptomatic, %	39.7	35.6	47.6	
Symptoms, %				
Palpitations	73.7	75.7	68.8	0.0021
Dyspnea	53.7	51.8	58.4	0.0082
Chest pain	23.5	22.8	25.1	0.3044
General non-well-being	34.9	34.1	36.8	0.2578
Dizziness	24.0	22.8	26.9	0.0632
Fatigue	46.7	47.2	45.4	0.4737
Fear/anxiety	12.2	13.3	10.1	0.0107
Heart rate, beats/min	90.1 ± 29.6	90.2 ± 29.5	90.0 ± 29.8	0.8090
Systolic AP, mm Hg	131.9 ± 20.6	131.1 ± 20.3	133.4 ± 21.3	0.0034
Diastolic AP, mm Hg	78.9 ± 12.7	79.6 ± 12.3	77.4 ± 13.4	<0.0001
EF, %	52.3 ± 13.5	52.2 ± 13.6	55.5 ± 13.2	0.7307
Hemoglobin, g/dl	13.6 ± 1.9	14.0 ± 1.8	12.9 ± 1.9	<0.0001
AF-QoL score				
Psychological domain	19.9 ± 8.0	19.9 ± 8.0	19.8 ± 8.2	0.7076
Physical domain	20.6 ± 9.5	21.4 ± 9.6	18.8 ± 9.0	<0.0001
Sexual activity domain	9.7 ± 4.2	9.8 ± 4.1	9.5 ± 4.5	0.3605
Total score	48.3 ± 20.0	49.5 ± 19.9	45.6 ± 19.8	<0.0001

Values are % or mean ± SD. *CHA_2DS_2-VASc score: low risk, score = 0 in males, score = 1 in females; moderate risk, score = 1 in males; high risk, score ≥2.

AF = atrial fibrillation; AF-QoL = atrial fibrillation quality-of-life questionnaire; AP = arterial pressure; COPD = chronic obstructive pulmonary disease; EF = left ventricular ejection fraction; EHRA = European Heart Rhythm Association; HFPEF = heart failure with preserved systolic function (EF >45%); TIA = transient ischemic attack.

DISCUSSION

This subanalysis of the EORP-AF Registry shows that about one-third of patients seen for AF in routine cardiological practice are ≥75 years of age, less frequently symptomatic, and more likely to have persistent or permanent AF and a burden of comorbidities. Further relevant findings are that in the elderly, routine diagnostic procedures are underused,

TABLE 2 Diagnostic Procedures and Interventions Performed or Planned at Enrollment, by Age Group

	Whole Cohort (n = 3,119)	Age <75 yrs (n = 2,068)	Age ≥75 yrs (n = 1,051)	p Value
Diagnostic procedures, %				
Transthoracic echocardiography	91.8	92.6	90.3	0.0278
Transesophageal echocardiography	11.3	14.1	5.8	<0.0001
Electrophysiological study	4.2	5.6	1.4	<0.0001
Thyroid hormone level - before	53.6	56.4	48.1	0.2276
Thyroid hormone level - now	40.6	37.5	46.2	0.1509
Thyroid hormone level - planned	23.7	23.7	23.7	0.9974
Coronary angiography	14.4	13.8	15.7	0.1365
Exercise test	7.8	9.8	4.0	<0.0001
Holter monitoring	17.0	18.1	14.8	0.0214
Other procedures	6.5	6.5	6.5	0.9953
Interventions performed or planned, %				
Electrical cardioversion	22.8	26.8	15.1	<0.0001
Pharmacological cardioversion	24.7	25.8	22.7	0.0554
Catheter ablation	7.4	10.5	1.4	<0.0001
Pacemaker implantation	4.7	3.2	7.4	<0.0001
ICD implantation	1.1	1.3	0.7	0.1268
Surgery	0.4	0.4	0.3	0.7598

Values are %. Before/now/planned = before/at/after study enrollment; catheter ablation = any ablation for atrial fibrillation treatment; thyroid hormone level = thyroid hormone level measurement.
ICD = implantable cardioverter-defibrillator.

the rate-control is the preferred management strategy, and OA are less used, with age in itself and CKD negatively influencing this therapeutic choice. Conversely, antiplatelet therapy is more frequently prescribed to older individuals, particularly when HAS-BLED score is high. Moreover, a higher proportion of elderly patients have unfavorable outcomes after only 1 year of follow-up.

In the general population, AF increases with age, with a prevalence up to 17.3% above age 75 years (21). In our analysis, the proportion of subjects ≥75 years (33.7%) was remarkably higher than the 12% prevalence of those >80 years of age in the EHS-AF (14). This difference may result from both the secular trend of ageing of the general population, and an increased awareness of the clinical impact of AF in older cohorts, potentially reducing a referral bias in the EHS-AF. In elderly populations, AF is often a comorbid condition, complicating the course of several acute and chronic diseases (22). In EORP-AF, patients age ≥75 years more frequently had a history of CAD, CKD, COPD, hypertension, previous hemorrhagic events, TIA, or valvular heart diseases. Even if ejection fraction and heart rate did not differ by age, older patients more often had CHF, which was frequently caused by CAD, with preserved systolic function. Accordingly, in the American Heart Association's Get With The Guidelines Heart Failure program, patients with CHF admitted with AF were older and more likely to present with diastolic dysfunction than those in sinus rhythm (23). Interestingly, our older patients had worse AF-QoL physical domain scores, confirming the major negative impact on functional capacity that AF has at older ages (2).

The general management strategy resulting from the EORP-AF Registry is in keeping with a recent subanalysis of the AFFIRM study, which confirmed that in the elderly a rate-control strategy may be associated with reduced mortality and hospitalizations, compared with a rhythm-control approach (24).

The lower use of diagnostic procedures in our elderly patients is more difficult to explain. This was observed even for transthoracic echocardiography, ECG Holter monitoring, and exercise stress test, which represent the first-line tools in AF assessment, as reported in the key data elements for measuring the clinical management of patients with AF (25). Interestingly, similar findings had also been noticed in the EHS-AF (14). The complexity of elderly patients and the need to decrease their in-hospital stay could justify this clinical behavior, as shown in a random-sample of 5,993 Medicare beneficiaries, where those with AF were less likely to receive OA or high standards of care, as identified by execution of an echocardiogram or thyroid function tests (26). These observations were further confirmed in the ORBIT-AF Registry, which demonstrated that several factors associated with advanced age (frailty, prior stroke-TIA, CKD, COPD, osteoporosis, or thyroid disease) could be responsible for underprescription of evidence-based therapies (27).

In the EORP-AF, OA were used less frequently in elderly patients. Nevertheless, compared with the EHS-AF (14), which was conducted 10 years before, the prescription rate of OA grew substantially, from an overall 67% (14) to about 81%, and this occurred in the older group as well. In the EHS-AF, OA were used in 68% and in 56% of those age 65 to 80 and >80 years (14), respectively, whereas in the EORP-AF, 76.7% of those age ≥75 years received OA. However, European clinical practice is not uniform, as shown by the ATA-AF registry enrolling 7,148 patients with AF with a mean age of 77 years, which in recent years found an average OA prescription rate of only 56.2% in subjects with $CHADS_2$ score ≥2, with cardiologists performing much better than internists (15). Similarly, the Loire Valley Atrial Fibrillation Project found that antithrombotic treatment followed guidelines in only 53% of cases (28).

In our elderly group, age in itself and CKD were inversely associated with the use of OA, whereas a higher HAS-BLED score increased the probability of

an antiplatelet drug prescription. Indeed, this reflects a persistent reluctance to prescribe OA to older patients, poorly justified in view of the demonstration that, compared with aspirin, warfarin is effective and safe even in patients ≥75 years of age (12) and that, with increasing age, the protective effect of OA against stroke increases, whereas that of aspirin decreases (29). In the ATRIA study cohort, the net clinical benefit of warfarin therapy remarkably increased with increasing age, and was maximal at ≥85 years of age (11). Indeed, the perception of an unacceptably high bleeding risk in the elderly may be unfounded. For example, the bleeding incidence in a large group of patients with a median age of 84 years, followed by OA clinics, was as low as 1.87 events per 100 patient-years (30). Moreover, antiplatelet agents are not fully benign drugs in the elderly, as shown in the WASPO trial in octogenarians in which aspirin caused more adverse events than warfarin (31).

Other observational studies (32) outlined the most important factors associated with underprescription of OA in the elderly with AF, and reiterated our finding of age per se resulting in a negative predictor of adherence to guidelines, suggesting that better models to stratify the bleeding risk are maximally needed to foster the prescription of OA to older patients with AF (33), in whom underprescription is associated with an unacceptable increase in the combined endpoint of cardiovascular death, thromboembolism, or major bleeding (34). The relatively low use of NOACs, and the high prescription rate of antiplatelet drugs in older patients in the EORP-AF Registry, deserves further discussion. Compared with warfarin, NOACs might offer increased net clinical benefit particularly in older persons, who are at higher risk of bleeding (35,36). In a meta-analysis of elderly subjects enrolled into NOACs trials, these drugs did not increase the incidence of clinically relevant bleeding (OR: 1.02; 95% CI: 0.73 to 1.43) but were more effective than conventional therapy to prevent stroke or systemic embolism (OR: 0.65; 95% CI: 0.48 to 0.87), with a number-needed-to-treat of 71 (36). In accordance with findings from the EHS-AF (14), aspirin and clopidogrel, alone or in combination, were more commonly used in our older cohort, despite current guidelines underlining that aspirin is poorly effective in preventing cardioembolic stroke, while being associated with a risk of major bleeding similar to that observed with OA, especially in the elderly (18).

TABLE 3 Drug Therapy at Discharge By Age Group

	Whole Cohort (n = 3,119)	Age <75 yrs (n = 2,068)	Age ≥75 yrs (n = 1,051)	p Value
Antithrombotic drugs, %				
No antithrombotic medication	3.7	4.5	2.0	0.0060
Any antithrombotic treatment	96.3	95.5	98.0	
Oral anticoagulants	80.8	82.8	76.7	0.0012
VKA	72.7	73.7	70.7	0.1484
Dabigatran	6.9	8.0	4.8	0.0097
Rivaroxaban	1.5	1.3	1.7	0.5035
ASA	34.9	31.1	42.8	<0.0001
Clopidogrel	13.3	11.3	17.5	0.0001
Clopidogrel/ASA	9.4	8.2	11.9	0.0070
Prasugrel	0.3	0.3	0.2	>0.9999
Ticagrelor	0.3	0.4	0.2	0.6709
LMW heparin	6.1	5.5	7.3	0.1210
Fondaparinux	0.1	0.1	0.2	0.5402
Antiarrhythmic drugs, %				
Antiarrhythmic drugs	37.9	41.7	29.8	<0.0001
Class IC	9.3	11.7	4.2	0.0001
Flecainide	3.5	4.8	0.8	<0.0001
Propafenone	5.8	6.9	3.4	0.0018
Class III	28.7	30.3	25.5	0.0280
Amiodarone	25.9	27.0	23.5	0.0899
Dronedarone	0.3	0.4	0.2	0.6709
Sotalol	2.9	3.3	2.2	0.1612
Other antiarrhythmics	0.1	0.1	0.2	0.5393
Other drugs, %				
ACE inhibitors	46.5	45.5	48.5	0.2190
ARBs	20.4	19.5	22.2	0.1580
Beta-blockers	71.5	72.8	68.8	0.0650
Digoxin	21.9	20.4	25.2	0.0152
Diuretics	57.3	50.4	71.7	<0.0001
Aldosterone blockers	29.9	26.9	36.3	<0.0001
DHP calcium-channel blockers	13.1	12.9	13.5	0.6863
Non-DHP calcium-channel blockers	5.8	4.8	7.9	0.0049
Statins	52.9	50.9	56.9	0.0121
Oral antidiabetics	15.1	14.8	15.5	0.6885
Insulin	6.4	6.0	7.5	0.2006
Thyroid-suppressing drugs	2.5	2.8	1.9	0.2130

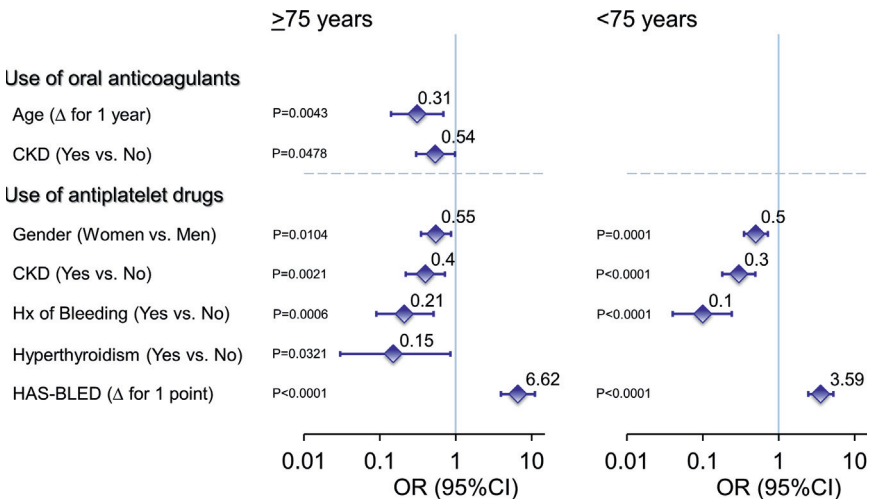
Values are %.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blockers; ASA = acetylsalicylic acid; DHP = dihydropyridine; LMW = low molecular weight; VKA = vitamin K antagonist.

STUDY LIMITATIONS. We arbitrarily selected an age ≥75 years to identify our "elderly" group. We cannot exclude that our results could have been different if we had chosen a more advanced age for stratification purposes. This selection bias might, for example, have contributed to having missed the demonstration of a protective effect of OA in our older cohort, whose worse 1-year prognosis was in fact, at multivariable analysis, associated only with age and several comorbidities (37).

Patients were enrolled in 70 centers across 9 European countries, which implies a potential inter-center and intercountry variability in the diagnostic and therapeutic strategies for AF. However, data collection confined in European regions might limit

FIGURE 1 Graphic Representation of the Predictors of the Use of Oral Anticoagulants and Antiplatelet Drugs by Age Group



Results of the multivariable models. No variables were associated with oral anticoagulants prescription in younger patients. CI = confidence interval; CKD = chronic kidney disease; Hx = history; OR = odds ratio. Δ = change of probability for the reported change of the independent variable.

the generalizability of our findings to other regions with different demographic structures, health services, and guidelines for disease management.

Because the qualifying AF episode might have occurred over 12 months before enrollment, we cannot exclude that such a wide time window might have influenced our findings on unfavorable event rates during the follow-up. However, the high proportion of patients with first detected or paroxysmal AF (56.8%) and with long-standing persistent or permanent AF (22.1%) should have reduced the impact of this potential source of bias.

Moreover, we have no data on the quality of OA therapy. However, our findings on antithrombotic therapy are qualitatively consistent with those obtained in the previous EHS-AF Registry (14). Finally, when baseline data were collected, NOACs had not yet received the authorization to be used in some countries.

TABLE 4 Predictors of Mortality at the 1-Year Follow-Up Using Logistic Regression Analysis*

	OR	95% CI	p Value
Age (≥75 vs. <75 yrs)	2.14	1.49–3.07	<0.0001
AF not as main diagnosis (yes vs. no)	2.84	1.90–4.25	<0.0001
CKD (yes vs. no)	3.52	2.43–5.11	<0.0001
COPD (yes vs. no)	1.62	1.05–2.50	0.0293
Malignancy (yes vs. no)	1.85	1.03–3.32	0.0410
Minor bleeding (yes vs. no)	2.37	1.36–4.13	0.0024
Previous TIA (yes vs. no)	2.48	1.36–4.54	0.0032
Diuretics (yes vs. no)	1.75	1.15–2.67	0.0091
Statins (yes vs. no)	0.61	0.43–0.87	0.0068
Oral antidiabetics (yes vs. no)	1.74	1.14–2.66	0.0108

*Predicted vs. observed classifications, concordant: 81%; $p < 0.0001$.

CI = confidence interval; CKD = chronic kidney disease; OR = odds ratio; other abbreviations as in Table 1.

CONCLUSIONS

The results of the present subanalysis of the EORP-AF Registry show that, in older patients, AF is associated with a more severe comorbidity profile. Rate control is the preferred therapeutic approach, many investigations are underused, and the use of OA is suboptimal in elderly subjects despite their higher CHA_2DS_2-VASc score. At follow-up evaluation, the incidence of adverse events is directly related to age and to comorbidities. These findings could be, at least in part, led by "ageism," a practice for which the rates of use of potentially lifesaving and life-enhancing investigations and interventions decline as patients get older (38), while the elderly are often excluded from randomized controlled trials (39). Accordingly, the management of patients with AF should change in the different phases of life but it should not be biased by age itself (40).

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REPRINT REQUESTS AND CORRESPONDENCE: Dr. Stefano Fumagalli, Division of Geriatric Cardiology and Medicine, Department of Experimental and Clinical Medicine, University of Florence and AOU Careggi, Viale Pieraccini 6, 50139 Florence, Italy. E-mail: fumadue@tin.it.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE 1: Clinical characteristics of patients referred for management of AF significantly differ by age.

COMPETENCY IN MEDICAL KNOWLEDGE 2: The diagnostic and therapeutic approach to patients with AF is strikingly different by age. Lower use of clinical tests and reduced prescription of oral anticoagulants are common in the elderly. Patients should be informed that oral anticoagulation is useful also at older ages.

TRANSLATIONAL OUTLOOK 1: Despite the observational design of our study, to increase the proper use of oral anticoagulants and to reduce the use of antiplatelet drugs in older patients with AF.

TRANSLATIONAL OUTLOOK 2: To start appropriate preventive strategies to improve survival in older patients with AF.

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