### Prevalence of Atrial Fibrillation and Use of Antithrombotics in Hypertensive Patients Aged ≥65 Years. The FAPRES Trial

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**Introduction and objectives.** Age and arterial hypertension are two of the main factors associated with atrial fibrillation and an increased risk of embolism. The objective of this study was to determine the prevalence of atrial fibrillation and the extent of antithrombotic use in hypertensive patients aged  $\geq$ 65 years in the Spanish region of Valencia.

**Methods.** Each study investigator enrolled the first three hypertensive patients aged  $\geq$ 65 years who came for a consultation on the first day of each week for 5 weeks. Each patient's risk factors, history of cardiovascular disease, CHADS<sub>2</sub> score and medical treatment were noted and an ECG was recorded. Data were analyzed centrally. A patient was regarded as having atrial fibrillation if it was observable on the ECG or reported in medical records.

**Results.** The study included 1,028 hypertensive patients with a mean age of 72.8 years. Overall, 10.3% had atrial fibrillation: in 6.7%, it was observable on the ECG while 3.6% were in sinus rhythm but had a history of the condition. Factors associated with atrial fibrillation were age, alcohol intake, structural heart disease and glomerular filtration rate. In total, 76.2% of patients with ECG evidence of atrial fibrillation and a CHADS<sub>2</sub> score >1 were taking anticoagulants compared with 41.7% of those who had a history of the condition but were currently in sinus rhythm.

**Conclusions.** The prevalence of atrial fibrillation in our group of hypertensives was 10.3%; in 1.7%, it was previously undiagnosed. Antithrombotic use was high in

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Received November 7, 2009. Accepted for publication February 22, 2010. patients with current atrial fibrillation, but lower in those who had experienced an episode previously.

Key words: Atrial fibrillation. Hypertension. Antithrombotic drugs.

### Prevalencia de fibrilación auricular y uso de fármacos antitrombóticos en el paciente hipertenso ≥ 65 años. El registro FAPRES

**Introducción y objetivos.** Entre los principales factores asociados a la presencia de fibrilación auricular y mayor riesgo embólico están la edad y la hipertensión arterial. Nuestro objetivo es conocer la prevalencia de fibrilación auricular en el paciente hipertenso de 65 o más años de edad en la Comunidad Valenciana y el empleo de fármacos antitrombóticos.

**Métodos.** Cada investigador incluyó a los primeros 3 pacientes hipertensos de edad  $\geq$  65 años que acudían a la consulta el primer día de la semana durante 5 semanas. Se recogieron los factores de riesgo, la historia cardiovascular, la puntuación CHADS<sub>2</sub> y el tratamiento farmacológico y se realizó un electrocardiograma para su análisis centralizado. Se consideró fibrilación auricular la que se detectó en el electrocardiograma y/o el antecedente documentado.

**Resultados.** Se incluyó a 1.028 pacientes hipertensos con una media de edad de 72,8 años. El 10,3% de los pacientes presentaban fibrilación auricular (el 6,7% en el electrocardiograma; el 3,6% estaba en ritmo sinusal, pero tenía antecedentes de la arritmia). Los factores asociados a fibrilación auricular fueron la edad, el alcohol, la cardiopatía estructural y el filtrado glomerular. Recibían tratamiento anticoagulante el 76,2% de los pacientes con fibrilación auricular conocida en el electrocardiograma y CHADS<sub>2</sub> > 1 y el 41,7% de los pacientes con antecedentes y en ritmo sinusal al momento del estudio.

**Conclusiones.** La prevalencia de fibrilación auricular en nuestra población hipertensa es del 10,3%, que no era conocida en el 1,7% de este grupo. La utilización de

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### ABBREVIATIONS

AF: atrial fibrillation ECG: electrocardiogram HT: hypertension LVH: left ventricular hypertrophy

fármacos antitrombóticos es elevada en los casos de fibrilación auricular actual conocida, pero se reduce en los pacientes con episodio previo.

**Palabras clave:** Fibrilación auricular. Hipertensión arterial. Fármacos antitrombóticos.

### **INTRODUCTION**

The prevalence of atrial fibrillation (AF) is increasing inexorably in recent years, owing to the aging population, the longer survival of patients with heart disease and, of course, the increased frequency with which it is diagnosed, among other factors, and it has become an important public health problem, especially because of the associated risk of stroke and mortality.<sup>1</sup>

The annual risk of stroke in patients with AF depends on the number of associated risk factors. Two of these major factors are age and hypertension (HT),<sup>2</sup> and, thus, it is essential to identify the patients in whom these 2 conditions coincide in order to adopt the proper preventive measures and diminish the cardioembolic events, occasionally asymptomatic, which can contribute to vascular dementia and to the deterioration of cognitive function in these patients.<sup>3</sup>

Despite the fact that a number of studies have demonstrated that oral anticoagulation reduces the risk of stroke by 66%, in routine practice, this treatment can be seen to be underutilized, especially in women and older patients, owing to the risk of bleeding and the need for periodic monitoring, among other factors.<sup>4,5</sup>

In Spain, there have been no recent studies analyzing the management of cardioembolic aspects in order to prevent this arrhythmia in the patient who is both hypertensive and elderly, two of the most prevalent conditions associated with AF and a higher risk of cardioembolism. The objective of this study was to determine the prevalence of AF in hypertensive patients 65 years and older receiving medical care in outpatient clinics and to analyze the use of antithrombotic drugs in this population.

### **METHODS**

The FAPRES registry resulted from a crosssectional, observational, multicenter epidemiological study, carried out in the health care setting, designed to determine the prevalence of AF in patients aged 65 years and over with a clinical diagnosis of HT in the Valencian Community in eastern Spain. The study took place between June and December, 2008. It involved the participation of 69 researchers from primary care and in-hospital HT units in the Spanish provinces of Alicante, Castellón, and Valencia, in a proportion in accordance with the population of each.

### **Study Population**

For the 5 weeks' duration of the recruitment period, each researcher included consecutively the first 3 patients who came to his or her office on the first day of the workweek, provided they met all the inclusion criteria and none of the exclusion criteria.

The inclusion criteria were: *a*) age  $\geq 65$  years; *b*) a previous diagnosis of HT at least 3 months prior to the start of the study (office arterial blood pressure  $\geq 140/90$  mmHg on several occasions or with previous antihypertensive therapy); and *c*) consent to participate in the study. The exclusion criteria were age <65 years, arm circumference >42 cm, refusal to consent to participate in the study or conditions that made the patient unfit to take part in the study (for example, evident failure to cooperate, dementia, etc).

Written informed consent was collected from all the patients and the study was carried out in compliance with the principles of the Declaration of Helsinki (Edinburgh amendment, 2000), after having been approved by the hospital ethics committee (Clinical Research Ethics Committee, Hospital General Universitario de Castellón).

### **Clinical Evaluation**

The risk factors and the cardiovascular history of the patients were gathered using a standardized questionnaire. We recorded the age in years, sex, anthropometric data, time elapsed since onset of HT, history of early cardiovascular disease in the immediate family (<65 years of age in women, <55 years of age in men) and personal history of high alcohol consumption, sedentary lifestyle, smoking, diabetes mellitus, dyslipidemia, structural heart disease (coronary artery disease or heart failure), previous stroke, peripheral artery disease, and renal disease.<sup>6</sup> The background data also included any previously documented episodes of AF in order to identify cases of paroxysmal or persistent AF that had reverted to sinus rhythm.

Any patient with a history of diabetes mellitus or who was receiving treatment for that disease at the time was considered to be diabetic. Those patients with a history of elevated low-density lipoprotein cholesterol (LDL-C) (>160 mg/dL) or who were receiving treatment involving their diet or lipid-lowering drugs were considered to have hypercholesterolemia.7 Patients who reported having consumed at least 1 cigarette a day for the preceding month were considered to be smokers.<sup>8</sup> In contrast, any patient who had stopped smoking at least one year earlier was considered to be an ex-smoker. Those who reported that they walked actively for at least 30 minutes a day or participated in some type of sport 3 days a week were considered nonsedentary,9 and patients who admitted to drinking 4 beers, 4 glasses of wine, 2 whiskies or similar beverages, or more, daily were considered to be drinkers.<sup>10</sup> Renal disease was considered to be present in those patients with a history of microalbuminuria (20-299 mg/24 h), proteinuria (300 mg/24 h or higher) or elevated serum creatinine (>1.2 mg/dL in women and >1.3 mg/dL in men).<sup>11</sup>

The drug therapy being received by each patient at the time of the visit, specifically antihypertensive agents and treatments to prevent cardioembolic events (anticoagulants and platelet antiaggregants), was recorded. A physical examination was also carried out to collect anthropometric data (weight, height and abdominal circumference); in addition, arterial blood pressure was taken on 2 consecutive occasions, and the mean of the 2 measurements was employed as the reference value. The analytical data were gathered from the medical record, if it was dated within the preceding 6 months, or were requested of the laboratory at the time of recruitment. The glomerular filtration rate was determined using the formula of the Modification of Diet in Renal Disease (MDRD) study. The questionnaire with the medical record was sent via CRD (the same platform utilized in the Cardiorisc project, available from: www. cardiorisc.com) to a data processing center.

All of the patients also underwent an electrocardiogram (ECG) that was sent by ordinary mail to a referral center, where two expert cardiologists who did not have access to the clinical data corresponding to the patients independently analyzed the cardiac rhythm. When there was a discrepancy between the 2, a third specialist was consulted. Other parameters analyzed in the ECG were the heart rate, the presence of left ventricular hypertrophy (LVH) (applying the Sokolov criteria, the Cornell criteria or ventricular overload), interventricular conduction disturbances and O waves indicative of myocardial necrosis. Α randomized external audit of 10% of the questionnaires received was carried out to verify the reliability of the data provided.

The group of patients with AF included all those in whom the ECG demonstrated the presence of said arrhythmia (regardless of whether or not it had been diagnosed previously) or who had a documented history of AF, even if they were in sinus rhythm at the time of the test and, thus, probably had paroxysmal or cardioverted AF. In the case of atrial flutter, the patient was included in the AF group, given that the antithrombotic recommendations are similar. Likewise, for the purpose of analyzing the antithrombotic therapy (anticoagulation or antiaggregant therapy) according to the type of AF, the patients with this arrhythmia were divided into 3 groups: a) patients with a history of AF in whom the arrhythmia was detected in the ECG (known permanent AF); b) patients with a history of AF and in sinus rhythm at the time of the test (previous episode of AF); and c) patients with no history of AF and with AF at the time of the ECG (previously undiagnosed AF). Finally, the patients' CHADS<sub>2</sub> scores (congestive heart failure, hypertension, age >75 years, diabetes mellitus, and prior stroke or transient ischemic attack) of the patients with AF were determined to assess the risk of stroke and the correct indication for anticoagulation therapy  $(CHADS_2 \text{ score } >1)$ .<sup>12</sup> The contraindications for anticoagulation were also recorded in the study.

### Statistical Analysis

All the data collected in the study are expressed in terms of central tendency, measures of dispersion and relative frequencies. The results in the three groups of patients analyzed were compared. Student t test was utilized for the comparison of the quantitative variables between the 2 major groups of individuals (those having and those not having AF); the categorical variables were compared using the  $\chi^2$  test, and we calculated the measures of effect (odds ratio [OR] for the categorical variables and the differences between means for the quantitative variables). In the comparative analysis of antithrombotic therapy according to the type of AF in the three groups, analysis of variance (ANOVA) was employed. To determine the variables independently related to the presence of AF (in the ECG or in a previous episode), we performed multivariate logistic regression analysis, including all the variables that proved to be significant in the univariate analysis and those with known clinical relevance. A P value of less than .05 was considered to indicate statistical significance. The analysis was carried out with the SPSS statistical software package (version 15).

Variable	Group Without AF (n=922)	Group With AF (n=106)	Measures of Effect <sup>a</sup>	Р
Age, mean (SD), y	72.5 (5.7)	75.8 (6)	3.34 (2.2-4.5)	<.001
Men, n (%)	430 (46.6)	56 (52.8)	0.78 (0.5-1.2)	.259
Smokers, n (%)	80 (8.7)	13 (12.3)	1.4 (0.8-2.7)	.213
Diabetes mellitus, n (%)	255 (27.7)	29 (27.4)	0.9 (0.6-1.5)	1
Hypercholesterolemia, n (%)	444 (48.2)	53 (50)	1.1 (0.7-1.6)	.759
Physical exercise, n (%)	348 (37.7)	24 (22.6)	0.5 (0.3-0.8)	.002
Alcohol consumption, n (%)	30 (3.3)	8 (7.5)	2.4 (1.1-5.4)	.049
Previous angina, n (%)	93 (10.1)	18 (17.1)	1.8 (1.1-3.2)	.045
Previous infarction, n (%)	51 (5.5)	16 (15.1)	3.1 (1.6-5.5)	.001
Coronary revascularization, n (%)	38 (4.1)	13 (12.6)	3.3 (1.7-6.5)	.001
leart failure, n (%)	35 (3.8)	39 (38.6)	15.8 (9.4-26.8)	<.001
Stroke, n (%)	64 (7)	12 (11.8)	1.8 (0.9-3.4)	.108
Renal failure, n (%)	52 (5.7)	10 (9.8)	1.8 (0.9-3.7)	.122
History of HT, mean (SD), y	10.7 (8)	12.8 (10)	2.12 (0.5-4.1)	.034

TABLE 1. Baseline Characteristics and History of the Population Analyzed, Grouped According to Whether or not
the Patients Had Atrial Fibrillation

AF indicates atrial fibrillation; HT, hypertension; SD, standard deviation.

<sup>a</sup>The measures of effect are the differences in means and odds ratio between the groups without and with AF, with the 95% confidence interval, for quantitative and qualitative variables, respectively.

### RESULTS

The study included a total of 1028 hypertensive patients, with a mean age of 72.8 years, 52.7% of whom were women. In all, 82.5% of the patients were recruited from primary care offices (848 cases) and the remainder from hospital HT units.

The analysis of the ECG revealed that 6.7% of the patients had AF (67 cases of AF and two of atrial flutter), and that the arrhythmia had not been previously diagnosed in 17 cases (1.7%). A linear increase was observed in the prevalence of AF in the ECG in relation to age, going from 3.2% in patients between the ages of 65 and 69 years to 11.9% in those over the age of 80 years. In addition, 37 patients in sinus rhythm had a history of AF (3.6%), which could correspond to paroxysmal or permanent forms reverted to sinus rhythm; thus, the total prevalence of AF in our series was 10.3%. The prevalence was significantly higher among the patients recruited from the HT units than among those from primary care (23.9% vs 7.4%; P<.001).

The mean age of the patients with AF (a previous episode or ongoing AF) was older and these individuals also were more likely to have a history of associated heart disease (ischemic heart disease or heart failure) and a longer history of HT (Table 1). Left ventricular hypertrophy and changes in the QRS complex were more common in this population. In contrast, the glomerular filtration rate was lower in the patients with AF (Table 2). When we analyzed the group of patients in whom AF had not previously been diagnosed (17 cases), we observed that they were significantly younger than the patients with known ECG evidence of AF (72.5 [3.6] years vs 76.7 [6.3] years; P<.05), exercised

more and were less likely to have a history of heart failure; in contrast, there were no differences with respect to the ventricular response in the ECG. This lesser clinical impact could probably justify in part the failure to detect the arrhythmia.

A large number of the patients received drugs to block the renin-angiotensin axis to control their HT. The figure shows the antihypertensive drugs employed in our population. No differences were observed between the subgroups analyzed, with the exception of the significantly greater use of beta blockers among the patients with AF (31.1% vs 18.4%; P<.01).

If we analyze the anticoagulation therapy according to the type of AF, we observe that the prevalence of anticoagulation among patients with known AF (52 cases) is 71.2%, whereas 3 of the 17 patients with previously undiagnosed AF (17.6%) received anticoagulation for other reasons (Table 3). The rate of anticoagulation in the group of patients with a previous episode of AF and in sinus rhythm at the time of the examination was 37.8% (14 patients). We observed that 73 of the 106 patients with AF had a CHADS<sub>2</sub> score >1 (68.9%), with a higher proportion (80.8%) in the group with persistent AF (Table 3). If we analyze the adjustment of the anticoagulation therapy as defined by the patients in whom anticoagulation is indicated by a CHADS<sub>2</sub> >1 and who are receiving treatment, we observe that 76.2% of the group with permanent AF, 41.7% of the group with a previous episode and 14.3% of the group with undiagnosed AF were correctly treated. Anticoagulation therapy was contraindicated in only three patients with AF (2.8%).

In the multivariate analysis, the factors associated

Variable	Group Without AF (n=922)	Group With AF (n=106)	Measures of Effect <sup>a</sup>	Р
Anthropometric variables				
Body mass index, mean (SD)	29.2 (4.2)	29.5 (4.5)	0.4 (-0.5-1.2)	.401
Abdominal circumference, mean (SD), cm	98.2 (11.4)	100 (13.5)	1.75 (-0.6-4.1)	.202
Office SAP, mean (SD), mmHg	147.1 (18.8)	143.6 (19.8)	-4.1 (-8.1-0.1)	.073
Office DAP, mean (SD), mmHg	81.4 (11.2)	78.8 (9.7)	-3.2 (-5.7-0.7)	.021
Laboratory analyses				
Leukocytes/µL, mean (SD)	6686 (1677)	7081 (2445)	394 (127-917)	.137
Hemoglobin, mean (SD), g/dL	13.6 (1.8)	13.7 (1.8)	0.12 (-0.3-0.5)	.505
Glucose, mean (SD), mg/dL	108 (31)	111 (32)	3.4 (-3.1-9.9)	.301
LDL-C, mean (SD), mg/dL	119 (34)	109 (33)	-12.4 (-17.1 to -2.9)	.006
Triglycerides, mean (SD), mg/dL	130 (74)	117 (63)	-13.1 (-26.3-0.9)	.088
Uric acid, mean (SD), mg/dL	5.2 (1.1)	5.4 (1.1)	0.3 (-0.1-0.5)	.058
Creatinine, mean (SD), mg/dL	0.96 (0.28)	1.06 (0.28)	0.1 (0.04-0.16)	.001
Glomerular filtration rate, mean (SD), mL/mi	in 75.8 (22.8)	68.2 (18.7)	-7.5 (-12.2 to -2.9)	.001
Albumin/creatinine ratio,b mean (SD)	40.1 (114)	34.2 (68.8)	-5.8 (-25.8-14.1)	.691
ECG				
Heart rate, mean (SD), bpm	71.2 (12.7)	76.5 (21.9)	5.3 (0.9-9.6)	<.001
Normal QRS, n (%)	723 (78.4)	71 (67)	0.6 (0.4-0.9)	.01
Q waves, n (%)	21 (2.3)	4 (3.8)	1.7 (0.6-4.9)	.316
LVH (Sokolov), n (%)	13 (1.4)	2 (1.9)	1.3 (0.3-6)	.662
LVH (Cornell), n (%)	86 (9.3)	17 (16)	1.9 (1.1-3.3)	.039
Ventricular overload, n (%)	66 (7.2)	18 (17)	2.6 (1.6-4.7)	.002
Overall LVH <sup>c</sup> , n (%)	149 (16.2)	28 (26.4)	1.9 (1.2-2.9)	.014

## TABLE 2. Clinical, Biochemical, and Electrocardiographic Parameters in Patients With and Without Atrial Fibrillation

AF indicates atrial fibrillation; DAP, diastolic arterial pressure; ECG, electrocardiogram; LDL-C, low-density lipoprotein cholesterol; SAP, systolic arterial pressure; SD, standard deviation.

<sup>a</sup>The measures of effect are the differences in means and odds ratio between the groups without and with AF, with the 95% confidence interval, for quantitative and qualitative variables, respectively.

<sup>b</sup>This result was available in 559 patients.

°Sokolov and/or Cornell and/or ventricular overload.

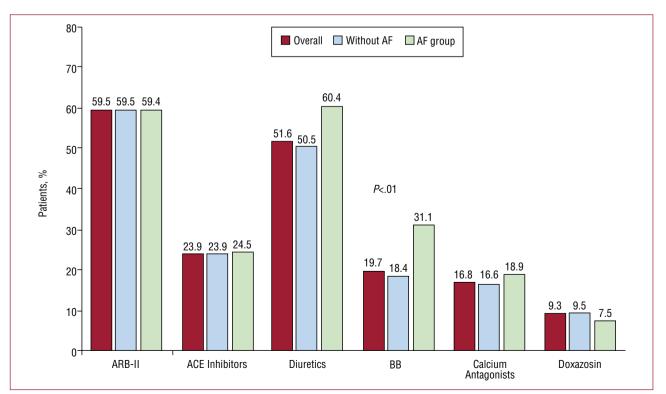


Figure 1. Antihypertensive treatments utilized in the population. Comparison according to subgroups. ACE indicates angiotensin converting enzyme; AF, atrial fibrillation; ARB, angiotensin receptor blockers (angiotensin II receptor antagonists); BB, beta-blockers.

	Total AF (n=106)	Permanent AF (n=52)	Previously Undiagnosed AF (n=17)	Previous AF Episode (n=37)	₽
CHADS <sub>2</sub> score, mean (SD)	2.29 (1.2)	2.56 (1.1)	1.76 (1.1)	2.16 (1.2)	<.05
CHADS <sub>2</sub> >1, n (%)	73 (68.9)	42 (80.8)	7 (41.2)	24 (64.9)	<.01
Oral anticoagulants, n (%)	54 (50.9)	37 (71.2)	3 (17.6)	14 (37.8)	<.001
Platelet antiaggregants, n (%)	19 (17.9)	2 (3.8)	6 (35.3)	11 (29.7)	.004
Anticoagulants + antiaggregants, n (%)	2 (1.9)	0	1 (5.9)	1 (2.7)	NS
Adequate treatment with acenocoumarol, n (%)b	43 (40.6)	32 (76.2)	1 (14.3)	10 (41.7)	<.001

FA:AF indicates atrial fibrillation; NS, not significant; SD, standard deviation.

<sup>a</sup>Comparisons between the 3 populations.

<sup>b</sup>Patients with a CHADS2 score >1, an indication for anticoagulation, who are receiving acenocoumarol.

# TABLE 4. Multivariate Analysis. Factors AssociatedWith Atrial Fibrillation on Electrocardiogramor a Previous Episode of Atrial Fibrillation

W. 2.11.	Atrial Fibrillation			
Variable	OR (95% CI)	Р		
Age	1.08 (1.04-1.12)	<.001		
Alcohol	5.33 (2.13-13.36)	<.001		
Physical exercise	0.61 (0.36-1.03)	.064		
Heart disease	4.73 (2.99-7.49)	<.001		
LVH due to overload	2.01 (1.07-3.78)	<.05		
Glomerular filtration rate	0.98 (0.97-0.99)	.016		

HVICI indicates confidence interval; LVH, left ventricular hypertrophy; OR, odds ratio.

The variables introduced into the model are: age, sex, smoking habit, diabetes mellitus, hypercholesterolemia, time elapsed since diagnosis of hypertension, history of heart disease (coronary artery disease and/or heart failure), previous stroke, alcohol consumption, physical exercise, glomerular filtration rate and LVH according to the Sokolov or Cornell criteria or ventricular overload.

with the presence of AF (during the ECG or a previous episode) were age, structural heart disease (coronary artery disease or heart failure), alcohol consumption and LVH due to ventricular overload (Table 4). In contrast, physical exercise was associated with a reduction in the risk of AF, nearly achieving significance.

### DISCUSSION

Our report is one of the few studies carried out in Spain that analyze the prevalence and the antithrombotic treatment of AF in a population characterized as being hypertensive and over 65 years of age, regardless of the type of AF (previous history or ongoing AF) and it demonstrated a total prevalence of 10.3%, with a very high rate of use of antithrombotic drugs, especially among the patients with known AF detectable in the ECG. Moreover, it reflects the fact that, in 1 of 4 patients with AF according to the ECG, the presence of said arrhythmia had not been detected, with the therapeutic and prognostic implications that this circumstance entails.

The CARDIOTENS 1999 study, with a crosssectional design and carried out in the primary care and specialized settings in Spain, showed an overall prevalence of chronic AF of 4.8%, which reached 11.1% among individuals of >80 years of age.<sup>13</sup> In this study, the diagnosis of AF was based on the background gathered from the medical records, as there was no protocol calling for the performance of an ECG, nor were the cases of paroxysmal or isolated AF recorded, a circumstance that may limit the estimate of the true prevalence of the arrhythmia. Atrial fibrillation is characterized by its temporal pattern, with periods in which the patient is in sinus rhythm; thus the need to search for this arrhythmia actively and repeatedly, especially in patients at risk, in order to reduce cardioembolic risk by means of the proper treatment. Another of the epidemiological studies carried out in Spain, the PREV-ICTUS study, involving a population of 7108 subjects over the age of 60 years (73% of them with HT), reported the observation of AF in the ECG of 8.5% of the patients, a prevalence that increases linearly with age, from 4.5% in subjects between the ages of 60 and 64 years to up to 16.5% in those over the age of 85 years.<sup>14</sup> In this analysis, the patients with a previous episode of AF were not taken into account. It is surprising that the incidence of AF according to the ECG findings was slightly higher than that documented in our study, despite the fact that the risk was higher in our population given that all the patients were hypertensive. Evidently, we can not compare these results because the analysis of the ECG in the PREV-ICTUS study was not centralized and the reading was carried out by one of the researchers, with the limitations that this circumstance can entail. One explanation that can justify this lower prevalence of AF in the ECG in our population is the high rate of use of drugs that block the renin-angiotensin-aldosterone axis for the treatment of HT. In this respect, numerous published studies have shown a reduction in the incidence of AF with the use of angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers

### (ARB).<sup>15,16</sup>

From a practical point of view, one of the major advances in the treatment of patients with AF over the past few decades has been the demonstration of the fact that the incidence of embolic episodes is reduced by the treatment of high-risk patients with anticoagulation therapy. In large randomized studies on the prevention of stroke in AF, the major associated risk factors were advanced age, female sex, previous stroke or transient ischemic attack, HT and diabetes mellitus.<sup>17</sup> A number of studies report rates of anticoagulation therapy in patients with AF of around 50%.<sup>18</sup> Our results reveal a very high rate of use of these drugs among patients with AF according to the ECG, especially in the group of known AF, surpassing that reported in other studies carried out a few years ago in Spain. In a subanalysis of the CARDIOTENS study performed in 999 patients with AF, the use rate of antithrombotic agents was 33%, with lower levels in the primary care setting, and significantly lower levels among the oldest patients,19 despite the fact that it is in the latter population that the greatest net benefit is produced.<sup>20</sup> The fear of falls and the risk of bleeding constitute the major limiting factor when it comes to deciding not to anticoagulate elderly patients.<sup>21</sup> In this respect, a study was recently published that indicates that anticoagulation therapy is acceptable in patients over 80 years of age given the low risk if adequate follow-up of the treatment is carried out.<sup>22</sup> This increase in the use of antithrombotic drugs in patients with AF over the past decade has also been corroborated in other countries.

A striking finding in our study is the lesser use of antithrombotic drugs in patients with previous episodes of AF who are in sinus rhythm and in whom they are indicated because of a CHADS<sub>2</sub> score >1 (41.7%), despite the fact that the latest guidelines clearly indicate that the subtype of AF should not influence the decision as to whether or not to anticoagulate a patient and that this decision should be based on the risk factors and contraindications.<sup>23</sup> This fact may reflect the limited awareness among physicians of the cardioembolic risk in these situations. Data from the Euro Heart Survey on Atrial Fibrillation corroborate this lower use of oral anticoagulation therapy in patients with paroxysmal AF (51%) with respect to those with persistent AF (80%) and permanent AF (76%), despite the fact that the researchers observed that the risk of stroke associated with paroxysmal AF is at least comparable to that found in persistent and permanent AF.24 These findings have also been confirmed by other studies carried out in different populations.<sup>25,26</sup>

### Limitations

One of the major limitations to studies of this type

is the number of subjects recruited and the degree to which our sample represents the universe of patients with this disease, since selection bias will always exist, taking into account the fact that the most seriously ill and motivated patients are those that usually come in contact with the health care system and are probably more highly represented in these studies. Despite this selection bias, our study shows the true management of the cardioembolic prevention of this arrhythmia in our setting, far from the large clinical trials. On the other hand, the cross-sectional nature of the study impedes the proper evaluation of cause and effect and can lead to unexpected associations, such as a better control of arterial blood pressure in patients with AF. Despite this circumstance, these limitations do not invalidate the results of our study, in which we analyze the presence of AF through the centralized analysis of the ECG in the hypertensive patient aged 65 years or older in a Mediterranean population.

### CONCLUSIONS

Our report shows a slightly lower prevalence of AF among hypertensive patients than that observed in other studies carried out in Spain, and reflects its strong association with advanced age, structural heart disease (including LVH according to the ECG) and alcohol consumption. In addition, it indicates a high rate of use of antithrombotic drugs (especially anticoagulants) among patients with known AF detected in the ECG, a circumstance that translates into a high awareness of the cardioembolic risk associated with this condition on the part of physicians. In contrast, less than half of the patients with a previous episode of AF and in sinus rhythm receive this treatment, despite their having a significant risk of stroke (CHADS<sub>2</sub> score <1).

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#### REFERENCES

- 1. Moro C, Hernández-Madrid A. Fibrilación auricular: ¿estamos ante una epidemia? Rev Esp Cardiol. 2009;62:10-4.
- Ruiz Ortiz M, Romo E, Mesa D, Delgado M, Anguita M, López Granados A, et al. Predicción de eventos embólicos en pacientes con fibrilación auricular no valvular: evaluación del *score* CHADS<sub>2</sub> en una población mediterránea. Rev Esp Cardiol. 2008;61:29-35.
- 3. Lip GY, Tse HF. Management of atrial fibrillation. Lancet. 2007;370:604-18.
- Lewis WR, Fonarow GC, Labresh KA, Cannon CP, Pan W, Super DM, et al. Differential use of warfarin for secondary stroke prevention in patients with various types of atrial fibrillation. Am J Cardiol. 2009;103:227-31.
- Srivastava A, Hudson M, Hamoud I, Cavalcante J, Pai C, Kaatz S. Examining warfarin underutilization rates in patients with atrial fibrillation: detailed chart review essential to capture contraindications to warfarin therapy. Thromb J. 2008;6:6.
- Llisterri-Caro JL, Rodríguez-Roca GC, Alonso-Moreno FJ, Banegas-Banegas JR, González-Segura D, Lou-Arnal S, et al. Control de la presión arterial en la población hipertensa española atendida en atención primaria. Estudio PRESCAP 2006. Med Clin (Barc). 2008;130:681-7.
- 7. Third report of the National Cholesterol Education Program (NCEP) Expert panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Circulation. 2002;106:3143-421.
- Consecuencias del tabaco para la salud. Informe técnico n.º 568. Ginebra: Organización Mundial de la Salud; 1974.
- Villar F, Maiques A, Brotons C, Torcal J, Lorenzo A, Vilaseca J, et al. Prevención cardiovascular en atención primaria. Aten Primaria. 2001;28 Supl 2:S13-36.
- 10. Anderson P, Cremona A, Paton A, Turner C, Wallace P. The

risk of alcohol. Addiction. 1993;88:1493-508.

- 11. 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2007;28:1462-536.
- Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA. 2001;285:2864-70.
- García Acuña JM, González Juanatey JR, Alegría E, González I, Llisterri JL. La fibrilación auricular permanente en las enfermedades cardiovasculares en España. Estudio CARDIOTENS 1999. Rev Esp Cardiol. 2002;55:943-52.
- 14. Cea-Calvo L, Redón J, Lozano JV, Fernández-Pérez C, Martí-Canales JC, Llisterri JL, et al. Prevalencia de fibrilación auricular en la población española de 60 o más años de edad. Estudio PREV-ICTUS. Rev Esp Cardiol. 2007;60:616-24.
- Blaauw Y, Crijns HJ. Atrial fibrillation: insights from clinical trials and novel treatment options. J Intern Med. 2007;262:593-614.
- 16. Wachtell K, Lehto M, Gerdts E, Olsen MH, Hornestam B, Dahlof B, et al. Angiotensin II receptor blockade reduces newonset atrial fibrillation and subsequent stroke compared to atenolol: the Losartan Intervention For End Point Reduction in Hypertension (LIFE) study. J Am Coll Cardiol. 2005;45:712-9.
- 17. Nattel S, Opie LH. Controversies in atrial fibrillation. Lancet. 2006;367:262-72.
- Lip GY, Edwards SJ. Stroke prevention with aspirin, warfarin and ximelagatran in patients with non-valvular atrial fibrillation: a systematic review and meta-analysis. Thromb Res. 2006;118:321-33.
- Bertomeu V, Morillas P, González-Juanatey JR, Alegría E, García-Acuña JM, Gonzalez-Maqueda I, et al. Empleo de fármacos antitrombóticos en pacientes hipertensos con fibrilación auricular crónica. Estudio CARDIOTENS 99. Med Clin (Barc). 2002;118:327-31.
- Singer DE, Chang Y, Fang MC, Borowsky LH, Pomernacki NK, Udaltsova N, et al. The net clinical benefit of warfarin anticoagulation in atrial fibrillation. Ann Intern Med. 2009;151:297-305.
- Niska R, Han B. Anticoagulation for patients with atrial fibrillation in ambulatory care settings. J Am Board Fam Med. 2009;22:299-306.
- Poli D, Antonucci E, Grifoni E, Abbate R, Gensini GF, Prisco D. Bleeding risk during oral anticoagulation in atrial fibrillation patients older than 80 years. J Am Coll Cardiol. 2009;54:999-1002.
- 23. Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation--executive summary: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). J Am Coll Cardiol. 2006;48:854-906.
- 24. Nieuwlaat R, Dinh T, Olsson SB, Camm AJ, Capucci A, Tieleman RG, et al. Should we abandon the common practice of withholding oral anticoagulation in paroxysmal atrial fibrillation? Eur Heart J. 2008;29:915-22.
- 25. Hohnloser SH, Pajitnev D, Pogue J, Healey JS, Pfeffer MA, Yusuf S, et al. Incidence of stroke in paroxysmal versus sustained atrial fibrillation in patients taking oral anticoagulation or combined antiplatelet therapy. J Am Coll Cardiol. 2007;50:2156-61.
- Friberg L, Hammar N, Rosenqvist M. Stroke in paroysmal atrial fibrillation: report from the Stockholm Cohort of Atrial Fibrillation. Eur Heart J. 2009 Jan 27 [Epub ahead of print]. doi: 10.1093.