Prevalence of Atrial Fibrillation in the Spanish Population Aged 60 Years or More. The PREV-ICTUS Study

Luis Cea-Calvo,^a Josep Redón,^b José V. Lozano,^c Cristina Fernández-Pérez,^d Juan C. Martí-Canales,^e José L. Llisterri,[†] Jorge González-Esteban,^a and José Aznar,^g on behalf of the investigators of the PREV-ICTUS study

^aDepartamento de Investigación Clínica, Merck Sharp and Dohme de España, Madrid, Spain ^bUnidad de Hipertensión Arterial, RECAVA, Hospital Clínico Universitario, Universidad de Valencia, Valencia, Spain

°Centro de Salud Serrería 2, Valencia, Spain

^dUnidad de Investigación, Hospital Clínico San Carlos, Madrid, Spain

^eCentro de Salud San Antonio, Motril, Granada, Spain

^fCentro de Salud Ingeniero Joaquín Benlloch, Valencia, Spain

⁹Unidad de Investigación, Hospital Marina Alta, Denia, Valencia, Spain

Introduction and objectives. The aims of this study were to determine the prevalence of atrial fibrillation in individuals aged 60 years or more in Spain using a random sample of the population and to identify associated factors.

Methods. An analysis of the PREV-ICTUS study, a randomized cross-sectional population-based study of individuals aged 60 years or more, was carried out. Data on demographic variables, cardiovascular risk factors, and cardiovascular disease were obtained from medical records. The diagnosis of atrial fibrillation was based on the patient's medical history and an electrocardiogram performed during the study.

Results. In the 7108 individuals studied (mean age, 71.9 [7.1] years, 53.6% female), the prevalence of atrial fibrillation was 8.5% (95% confidence interval [CI], 7.9-9.2%). It was higher in males (9.3% vs 7.9% in females; P=.036) and increased from 4.2% in individuals aged 60-64 years to 16.5% in those aged 85 years or more (χ^2 test for linear trend, P<.001). Multivariate analysis showed that existing cardiovascular disease, hypertension, age, and left ventricular hypertrophy had the strongest associations with atrial fibrillation. Although there was a strong relationship between hypertension and atrial fibrillation (odds ratio, 2.53; 95% CI, 1.60-4.01), no association was found between poor blood pressure control and atrial fibrillation. A weak association with diabetes mellitus was found only when arterial pressure was included in the model, but not when a diagnosis of hypertension was included.

The PREV-ICTUS study was financed with a research grant from Merck Sharp and Dohme, Spain.

Correspondence: Dr. J. Redón. Unidad de Hipertensión Arterial. Hospital Clínico Universitario. Avda. Blasco Ibáñez, 17. 46010 Valencia. España. E-mail: josep.redon@uv.es

Manuscript received November 28, 2006. Accepted for publication March 1, 2007.

616 Rev Esp Cardiol. 2007;60(6):616-24

Conclusions. In this cross-sectional population-based study of elderly individuals, the prevalence of atrial fibrillation was 8.5%, and was strongly associated with existing cardiovascular disease, hypertension, age, and left ventricular hypertrophy.

Key words: Atrial fibrillation. Prevalence. Cardiovascular disease. Systemic arterial hypertension. Population-based studies.

Prevalencia de fibrilación auricular en la población española de 60 o más años de edad. Estudio PREV-ICTUS

Introducción y objetivos. El objetivo de este estudio fue analizar la prevalencia de fibrilación auricular (FA) en sujetos \ge 60 años en España y los factores asociados, en una muestra aleatoria de base poblacional.

Métodos. Análisis del estudio PREV-ICTUS, estudio transversal de base poblacional en sujetos ≥ 60 años. Se recogieron datos demográficos, factores de riesgo y enfermedades cardiovasculares. La FA fue diagnosticada por la historia médica y un electrocardiograma realizado en el momento del estudio.

Resultados. En 7.108 sujetos (edad media 71,9 ± 7,1 años, el 53,6%, mujer), la prevalencia de FA fue del 8,5% (intervalo de confianza [IC] del 95%, 7,9-9,2), mayor en varones (del 9,3%, frente al 7,9% en mujeres; p = 0,036) y aumentó desde el 4,2% en sujetos de 60-64 años al 16,5% en los \ge 85 años (χ^2 de la tendencia lineal; p < 0,001). En los modelos multivariables, la enfermedad cardiovascular establecida, la hipertensión, la edad y la hipertrofia ventricular izquierda tuvieron la asociación más fuerte con la FA, mientras que la hipertensión se relacionó con fuerza con la FA (odds ratio [OR] = 2,53; IC del 95%, 1,60-4,01) y no encontramos asociación entre peor control de la presión arterial y FA. La diabetes mellitus únicamente se asoció débilmente cuando en el modelo se introdujeron los valores de presión arterial y no el diagnóstico de hipertensión.

Conclusiones. En este estudio poblacional en sujetos de edad avanzada, la prevalencia de FA fue del 8,5% y se asoció con fuerza con la presencia de enfermedad cardiovascular, la hipertensión, la edad y la hipertrofia ventricular izquierda.

Palabras clave: Fibrilación auricular. Prevalencia. Enfermedad cardiovascular. Hipertensión arterial sistémica. Estudios de base poblacional.

ABBREVIATIONS

ECG: electrocardiogram AF: atrial fibrillation HT: hypertension LVH: left ventricular hypertrophy CI: confidence interval OR: odds ratio BP: blood pressure

INTRODUCTION

Atrial fibrillation (AF) is the most frequently encountered arrhythmia in clinical practice. Its prevalence is closely associated with older age^{1,2}; indeed, 70% of the cases of AF occur in patients over 65 years of age.² When AF develops, the risk of cardiovascular and cerebrovascular complications is greater and survival is shorter.³ Atrial fibrillation is an independent risk factor for developing stroke, which is between 3 and 5 times more likely to occur when AF is present.⁴ In patients aged 80 years or over, AF is the direct cause of 23.5% of episodes of stroke.⁴ Furthermore, in the general population, mortality is twice as high in individuals with AF.⁵⁻⁷

The prevalence of AF is increasing due to the aging population and the better survival of patients with heart disease; over the past 20 years, it is estimated that admissions to hospital due to AF have increased by 66%.⁸ In the coming years, the progressive aging of the population may lead to an increase in the prevalence of age-related diseases, such as arterial hypertension (HT) and AF, and their more serious consequences, such as stroke. Preventative measures will therefore be essential to reduce the burden on the health services that could arise from AF.

In Spain, however, there are no population-based studies that have analyzed the prevalence of AF in older individuals and what factors are associated with this arrhythmia. Studies of prevalence of AF in Spain have been performed in limited areas.⁹⁻¹¹ The CARDIOTENS study,¹² the largest study to date, reported an overall prevalence of AF of 4.8%, which increased for every 10 years of life (1.0% in those <50 years old, 11.1% in individuals \geq 80 years old). However, that study

consecutively included patients who attended appointments in primary health care facilities or cardiology clinics, and so it cannot be considered a population-based study.

The objective of this analysis of the PREV-ICTUS study was to assess the prevalence of AF in Spain in individuals aged 60 years or older, and the factors associated with this arrhythmia, in a randomized sample of individuals representative of the general population.

METHODS

This study analyzed the population included in the PREV-ICTUS study, which was an epidemiological, cross-sectional, multicenter, population-based study, designed to assess the risk of stroke in the Spanish population aged 60 years or older.¹³ The study was approved by an independent ethics committee for research and carried out by approximately 1200 researchers in primary health care facilities throughout Spain. Between September and December 2005, participating physicians collected information on 6 subjects selected at random from their registered patients.

Selection of Participants

The study included individuals aged 60 years or more who agreed to participate after receiving information about the study and signing a consent form. For the selection procedure, the overall sample size was calculated, and the number of subjects to be included in the study was distributed initially by autonomous regions according to the number of inhabitants aged 60 years or over in each region. Then, within each autonomous region, the same procedure was repeated for each province. Once the population had been distributed by provinces, a random selection was made of health centers and clinics, also taking into account the population distribution according to those living in an urban environment (>20 000 inhabitants), semiurban environment (5000-20 000), and rural environment (<5000). Health centers was selected from data sources published by the different local health authorities of each autonomous region by assigning a random number to each center. This number was obtained using Visual Basic functions ("Rnd ()" and "Randomize") and specific software was programmed in each case.

One investigator participated in each center selected. To perform a random selection of individuals from each physician's list of patients, the investigators obtained an alphabetical list of individuals aged 60 years or more from their list of patients, and assigned 6 random numbers, which corresponded to the 6 subjects they were to ask to participate in the study. The subjects were asked to participate by telephone. In the event that physicians were unable to contact the patient, the investigators had a reserve list of random replacement numbers. At all times, confidentiality was respected and the only people who could identify the patient were the investigators themselves.

Procedures

Once the individual had been included in the study, demographic and anthropometric data were collected along with risk factors and history of cardiovascular disease. Subjects were considered to be smokers if they were smokers at the time of the appointment or if they had given up less than 1 month earlier. Patients were considered not to drink alcohol if they never consumed regularly. If they consumed alcohol regularly, their intake was classed as low (<20 g/day in women or <40 g/day in men), moderate (20-39 g/day in women and 40-59 g/day in men), or high (\geq 40 g/day in women and \geq 60 g/day in men). Individuals were considered active or not sedentary if they were working or performed at least moderate exercise (for example, walking for half an hour a day). If available, biochemical data were taken from a medical record from the previous 6 months, otherwise a sample was taken for laboratory analysis at that visit. Renal function was estimated from glomerular filtrate calculated with the MDRD formula.14

Arterial blood pressure (BP) was obtained with the OMRON M6 blood pressure monitor in accordance with the recommendations of the main scientific societies. According to diagnosis of HT and BP readings, the population was classified into known hypertensive subjects (with diagnosis of HT or taking antihypertensive medication), subjects with high BP without diagnosis of HT (and who did not take antihypertensives), and normotensive subjects (with normal BP and no history of HT and not taking antihypertensives). Patients were considered diabetic if they were receiving oral antidiabetic agents or insulin or if they had fasting glucose levels greater than or equal to 126 mg/dL.

One electrocardiogram (ECG) was performed according to protocol. Left ventricular hypertrophy (LVH) was considered to be present if the patient met the Cornell voltage criteria¹⁵ or the Sokolow-Lyon criteria.¹⁶ All investigators recorded whether the participants had AF or not in the ECG. Diagnosis of AF was performed by each investigator according to the ECG reading. In addition, the investigators also recorded whether patients had a history of AF. This information would give an indication of cases with paroxysmal or persistent AF that had reverted to normal sinus rhythm. Nevertheless, for the purposes of establishing the comparative groups and performing the multivariate analysis, subjects were only included if they had evidence of AF in the ECG taken during the study visit and that AF was probably persistent or chronic, regardless of the history recorded by the investigators. The presence of any type of heart disease was defined according to the medical history of the patients. Patients were considered to have cardiovascular disease if they had at least one of the following in their

medical history: myocardial infarction, angina pectoris, heart failure, cerebrovascular disease, or intermittent claudication.

Statistical Analysis

The sample size calculation was performed for the primary study objective, which was to calculate the estimated risk of stroke at 10 years in the general Spanish population using the Framingham-D'Agostino scale¹³ and assuming a 50% risk probability (which would imply a larger sample size). For the sample distribution according to autonomous regions and centers, the latest population data published by the National Statistics Institute for 2003 were used.¹⁷ For a 95% certainty and an error of 1%, the sample size was calculated to be 6468 inhabitants. This increased to 7762 on assuming a 20% loss.¹³

The continuous variables were described as means (SD), and categorical ones as absolute frequencies and percentages. The results were compared between groups of individuals according to whether or not AF was present in the ECG and these groups were related to one another according to demographic and clinical variables. For the simple group comparison, we used the Student *t* test for independent groups or an analysis of variance if another categoric factor was considered. When categoric variables were tested, the χ^2 test was used.

Two logistic regression models were fitted to study the epidemiological profile of the subjects with AF. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. In all statistical tests, the null hypothesis was rejected when the alpha error was less than .05. Version 13.0 of the SPSS statistical package was used to process the data.

RESULTS

Descriptive Data

A total of 7555 individuals were evaluated; 447 (5.9%) were excluded because they failed to meet one of the inclusion criteria or because they did not have reliable ECG examinations. The present analysis therefore included 7108 subjects. The data of the final sample, distributed according to autonomous region, province, and type of environment, were adjusted to the theoretical population distribution.

The mean age of the subjects analyzed was 71.9 (7.1) years; 53.6% were women and 46.4% were men. Rural areas accounted for 27.8% of the subjects, semiurban areas for 19.6%, and urban areas for 52.6%. The mean body mass index (BMI) was 28.8 (4.4) and the abdominal circumference was 99.0 (13.6) cm. Overall, 34.7% were obese (BMI≥30) and only 18.4% had normal weight. Sedentary lifestyle was reported in 53.7%; 10.1% were active smokers and 26.1% were ex-smokers. Alcohol was

consumed regularly by 36.4% (28.2% reported mild consumption, 7.5% moderate consumption, and 0.6% heavy consumption). Hypertension had been diagnosed previously in 73.0%; 12.8% did not have a history of HT but had high BP at the time of the examination and 14.3% had normal BP. Diabetes mellitus had been diagnosed in 27.1%. Left ventricular hypertrophy was observed in the ECG in 12.5% of the subjects (10.8% according to the Cornell voltage criterion and 8.1% according to the Sokolow-Lyon criterion), and 25.7% presented abnormal renal function (glomerular filtration <60 mL/min/1.73 m²). Established cardiovascular disease was present in 1705 subjects (24.0% of the sample; 5.8% with myocardial infarction, 9.9% with angina pectoris, 8.3% with heart failure, 7.5% with cerebrovascular disease, and 5.1% with intermittent claudication).

The mean systolic BP was 143.6 (17.6) mm Hg and the mean diastolic BP was 80.6 (9.7) mm Hg. Of the nondiabetic subjects, 43.5% had BP below 140/90 mm Hg, and 13.0% of diabetic patients had BP below 130/80 mm Hg. Overall, 35.3% of the subjects had attained treatment goals for BP. Among the individuals diagnosed with HT, 28.7% had had attained treatment goals for BP.

Prevalence of Atrial Fibrillation

Atrial fibrillation was observed in the ECG in 605 subjects (prevalence of 8.5%; 95% CI, 7.9-9.2). Table 1 shows the prevalence of AF by age group and sex. The prevalence increased linearly from 4.2% in subjects aged

between 60 and 64 years to 16.5% in those aged 85 years or older (χ^2 test of linearity was significant; *P*<.001). The prevalence was slightly higher in men than in women (9.3% vs 7.9%; *P*=.036). In all age groups, prevalence was higher in men, except for subjects aged 85 years or more. Overall, 54% of the cases of AF were observed in the population aged 75 years or more (49% of men and 59% of women). Eighty-eight additional subjects (1.2%) were in sinus rhythm but had a history of AF and so could have had paroxysmal forms or permanent forms that had returned to sinus rhythm. In contrast, 80 subjects (1.1%) had AF in the ECG that had not been previously detected —these were probably cases of asymptomatic AF.

Table 2 shows the prevalence of AF according to the characteristics of the participants. The prevalence of AF was higher in subjects with known HT compared to those with normal BP or those who had high BP without prior diagnosis of HT (P<.001), in diabetic patients compared to nondiabetic patients, in patients with LVH, and in patients with abnormal renal function (P < .001 for all comparisons). In patients with a history of cardiovascular disease, 20.9% had AF compared to only 4.6% in those without a history of cardiovascular disease (P<.001). In addition, prevalence was higher in rural areas, among ex-smokers, and among those with a sedentary lifestyle, without significant differences with regard to the categories of BMI, alcohol consumption, or BP control. In subjects without cardiovascular disease and without HT or diabetes (subjects in whom AF would presumably be idiopathic), the prevalence of AF was 3.2%.

TABLE 1. Prevalence of Atrial Fibrillation According to Age and Sex: PREV-ICTUS Study*

	Atrial Fibrillation, No. of Cases/N, Prevalence, % (95% CI)			
	Overall	Men	Women	Р
60-64 years	56/1331, 4.2 (3.1-5.3)	33/637, 5.2 (3.4-7.0)	23/693, 3.3 (1.9-4.7)	.091
65-69 years	100/1735, 5.8 (4.6-6.9)	56/852, 6.6 (4.9-8.3)	44/880, 5.0 (3.5-6.5)	.161
70-74 years	122/1680, 7.3 (6.0-8.5)	67/786, 8.5 (6.5-10.5)	55/892, 6.2 (4.5-7.8)	.063
75-79 years	177/1378, 12.8 (11.0-14.6)	84/608, 13.8 (11.0-16.6)	93/766, 12.1 (9.8-14.5)	.357
80-84 years	104/705, 14.8 (12.1-17.4)	51/284, 18.0 (13.3-22.6)	52/420, 12.4 (9.1-15.7)	.04
>84 years	46/279, 16.5 (12.0-21.0)	14/127, 11.0 (5.2-16.9)	32/151, 21.2 (14.3-28.0)	.023
Total	605/7108, 8.5 (7.9-9.2)	305/3294, 9.3 (8.3-10.3)	299/3802, 7.9 (7.0-8.7)	.036

*Cl indicates confidence interval. χ^2 linear trend for age: P<.001.

In 12 cases, the sex of the subject was not reported.

TABLE 2. Prevalence of Atrial Fibrillation by Subgroup: PREV-ICTUS Study*

	Prevalence, %	Р
Sex Male Female	9.3 7.9	.036
Type of residential environment Rural Semiurban Urban	10.6 7.5 7.8	.001
Sedentary lifestyle No Yes	7.2 9.6	<.001
Smoking habit Never Ex-smokers Smokers	8.0 10.7 6.0	<.001
Alcohol consumption No Mild Moderate-heavy	8.5 9.0 7.7	.806
Blood Pressure Normal blood pressure High blood pressure without documented H HT	2.4 T 2.6 10.8	<.001
Diabetes mellitus No Yes	7.5 11.3	<.001
Blood pressure treatment goals attained#t No Yes	8.7 8.3	.565
Body mass index <25 25-29.9 ≥30	7.8 8.8 8.9	.557
Left ventricular hypertrophy No Yes	6.8 20.6	<.001
Abnormal renal function (GF<60 mL/min/m²) No Yes	7.1 12.9	<.001
History of heart disease No Yes	4.6 20.9	<.001

*GF indicates glomerular filtration; HT, hypertension.

+<140/90 mm Hg, and in diabetic patients <130/80 mm Hg.

Characteristics of Individuals With Atrial Fibrillation

Table 3 shows the characteristics of study subjects with and without AF in the ECG. The subjects with AF were

TABLE 3. Electrocardiographic Characteristics of the Subjects With and Without Atrial Fibrillation: PREV-ICTUS Study*

	Subjects Without AF (n=6503)	Subjects With AF (n=605)	Р
Age, years, mean (SD)	71.6 (7.0)	75.0 (7.1)	<.05
Women, %	54.0	49.5	<.05
Body mass index, mean (SD)	28.8 (4.4)	29.0 (4.6)	NS
Sedentary lifestyle, %	53.0	61.0	<.001
Smoking habit Never, % Ex-smokers, % Smokers, %	64.1 10.4 25.5	60.2 7.1 32.7	<.001
SBP, mm Hg, mean (SD)	143.4 (17.6)	141.8 (17.4)	<.05
DBP, mm Hg, mean (SD)	80.7 (9.6)	79.9 (10.3)	<.05
Diagnosed HT, %	71.2	92.1	<.001
Blood pressure treatment goal attained†, %	35.4	34.2	NS
Diabetes mellitus, %	26.2	35.9	<.001
GF mL/min/1.73 m ² , mean (SD)	75.0 (24.8)	68.1 (20.9)	<.05
Abnormal renal function (GF<60 mL/min/m ²), %	24.5	38.7	<.001
Left ventricular hypertrophy, %	10.9	30.2	<.001
History of heart disease, %	20.7	59.0	<.001

*AF indicates atrial fibrillation; GF, glomerular filtration; HT, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure. +<140/90 mm Hg, and in diabetic patients <130/80 mm Hg.

characterized by being older, having a higher percentage of women, being more sedentary, having more exsmokers, diagnosis of HT, diabetes mellitus, LVH in the echocardiographic examination, and decreased renal function. Among the individuals with AF, 91.1% were hypertense and 3.8% had high BP with no history of HT compared to 71.2% and 13.6%, respectively, among subjects without AF (P<.001). Overall, 60.1% of the subjects with AF were receiving anticoagulant therapy, 31.1% were only receiving antiplatelet therapy, and 8.8% were not taking any antithrombotic therapy. The prevalence of established cardiovascular disease was 59.0% in subjects with AF and 20.7% in those without AF (P<.001). The prevalence of any manifestation of

TABLE 4. Prevalence of Different Manifestationsof Cardiovascular Disease in Subjects Withand Without Atrial Fibrillation:PREV-ICTUS Study*

	Subjects Without AF (n=6503)	Subjects With AF (n=605)	Р
Cardiovascular disease (any), %	20.7	59.0	<.001
Angina pectoris, %	8.8	21.0	<.001
Myocardial infarction, %	5.4	10.3	<.001
Intermittent claudication, %	4.6	10.0	<.001
Heart failure, %	5.8	35.5	<.001
History of CVD, %	6.4	19.4	<.001

*AF indicates atrial fibrillation; CVD, cerebrovascular disease.

TABLE 5. Factors Independently Associated With Atrial Fibrillation: Multivariate Analysis of PREV-ICTUS Study*

Model 1†	OR (95% CI)	Р
Age, years		
65-69	1.32 (0.91-1.91)	.144
70-74	1.55 (1.08-2.23)	.018
75-79	2.51 (1.77-3.56)	<.001
80-84	2.52 (1.72-3.71)	<.001
85	2.45 (1.52-3.95)	<.001
Rural environment	1.25 (1.01-1.54)	.036
Ex-smoker	1.45 (0.99-2.12)	.06
Sedentary lifestyle	1.18 (0.98-1.43)	.086
Diagnosed hypertension	2.53 (1.60-4.01)	<.001
Uncontrolled blood pressure	0.82 (0.67-1.01)	.066
Abnormal renal function (GF<60 mL/min/m²)	1.37 (1.12-1.67)	.002
Left ventricular hypertrophy	1.81 (1.45-2.25)	<.001
Established cardiovascular disease	3.69 (3.03-4.51)	<.001

*GF indicates glomerular filtration (in mL/min/1.73 m²); OR (95% CI), odds ratio (95% confidence interval).

⁺Model 1: includes the variables sex, age (5-year intervals), environment, smoking habit, sedentary lifestyle, diagnosis of hypertension, control of blood pressure, diabetes mellitus, left ventricular hypertrophy, abnormal renal function, and established cardiovascular disease.

cardiovascular disease was higher among subjects with AF compared to those without AF (P<.001 for all comparisons) (Table 4). Blood pressure was slightly lower in patients with AF, whereas the percentage of subjects who had attained their BP goal was similar. A higher percentage of patients with AF lived in a rural environment.

Multivariate Analysis

To assess which factors were independently associated with AF, a multivariate model was constructed which included the variables age (in 5-year intervals), sex, type of environment, smoking habit, sedentary lifestyle, diagnosis of HT, BP control, diagnosis of diabetes mellitus, presence of LVH, abnormal renal function (glomerular filtrate <60 mL/min/m²), and established cardiovascular disease (Table 5). In this model, only patients with established diagnosis of HT were considered hypertense. Patients with normal BP and those with high BP without previous diagnosis of HT were considered as not hypertense. A positive and independent association was observed between the presence of AF and older age, living in a rural area, diagnosis of HT, LVH in the ECG, abnormal renal function, and established cardiovascular disease. An association was observed on the borderline of significance (P=.066) between attaining BP goals and the presence of AF, as well as between presence of AF and being an ex-smoker and sedentary lifestyle. The association between AF and age was observed particularly in groups aged 75 years or more (OR approximately 2.5 compared to individuals aged 60-64 years). No significant independent association was observed between diagnosis of diabetes mellitus and presence of AF. The adjusted OR are shown in Table 5 along with the confidence intervals.

In an alternative model, the same variables were included and diagnosis of HT and adequate BP control were replaced by systolic and diastolic BP as continuous variables (Table 6). In this model, a significant independent association was observed between prevalence of AF and older age, living in a rural environment, LVH in the ECG, abnormal renal function, and established cardiovascular disease. The association between AF and systolic BP was an inverse one (higher prevalence of AF corresponded to lower systolic BP), whereas the association in the case of diastolic BP was a direct one. With this model, a weak association was observed between AF, diabetes mellitus, and the condition of ex-smoker (Table 6).

DISCUSSION

In this analysis of the PREV-ICTUS study, we describe the prevalence of AF in a population-based sample of individuals aged 60 years or over in Spain. To the best of our knowledge, this is the first study of the prevalence of AF in Spain to use a population-based sample that is reasonably representative of the Spanish population, although in this case limited to subjects aged 60 years or over. The selection of subjects for the study was done by randomized selection of health centers and subjects from a list patients in accordance with the distribution of the population in the autonomous regions and even according to the type of environment (rural, urban, or semiurban). Given that in Spain, health coverage is almost

TABLE 6. Factors Independently Associated With Atrial Fibrillation: Multivariate Analysis of PREV-ICTUS Study*

Model 2†	OR (95% CI)	Р
Age, years		
65-69	1.31 (0.91-1.88)	.148
70-74	1.58 (1.10-2.25)	.012
75-79	2.70 (1.92-3.81)	<.001
80-84	2.84 (1.94-4.15)	<.001
≥85	2.61 (1.64-4.16)	<.001
Rural environment	1.30 (1.06-1.60)	.012
Ex-smokers	1.44 (0.99-2.10)	.06
Systolic blood pressure	0.99 (0.98-0.99)	<.001
Diastolic blood pressure	1.01 (1.00-1.02)	.060
Diabetes mellitus	1.18 (0.97-1.44)	.090
Abnormal renal function (GF <60 mL/min/m ²)	1.37 (1.13-1.68)	.001
Left ventricular hypertrophy	1.91 (1.54-2.37)	<.001
Established cardiovascular disease	4.08 (3.36-4.97)	<.001

*GF indicates glomerular filtration (in mL/min/1.73 m²); OR (95% CI), odds ratio (95% confidence interval).

universal, this selection procedure can be considered reasonably representative of the Spanish population aged 60 years or over.

The prevalence of AF was 8.5% (95% CI, 7.9-9.2) and slightly higher in men and older subjects. According to census data, the population aged 60 years or more totals 9 million¹⁷; thus we estimate that between 720 000 and 840 000 patients in Spain have AF. The prevalence was markedly higher for age groups older than 75 years. For the year 2026, the number of persons aged 65 years or more is expected to increase to 23%.¹⁸ In addition, a tendency over time towards increased prevalence of AF has been observed, both in men and women, even after adjustment for other factors such as age.¹⁹⁻²¹ This suggests that the number of cases of AF and the risk of associated complications could increase in the future, becoming a huge burden on the Spanish health system. Therefore the definition and application of preventative measures are also necessary for this disease. The prevalence observed in our study, particularly among older persons, is in agreement with that observed in other studies.^{1-3,12,22,23}

The factors most strongly associated with greater prevalence of AF were older age (particularly age of 75 years or more), evidence of established cardiovascular disease, diagnosis of HT, and evidence of LVH in the ECG. Atrial fibrillation is a disease typically found in older subjects, and the studies of incidence and prevalence of AF show a strong association with age. Furthermore, the findings of other studies have already suggested that the association with established cardiovascular disease is strongest.²⁴

Our study also shows a strong association of AF with diagnosis of HT (Table 5), but not with BP levels or degree of BP control (Table 6). Although the relative risk of AF associated with HT is not very high (1.4-2.1), it has been postulated that HT, in view of its high prevalence, is the most important risk factor (and the most modifiable) for development of AF.²⁵ In this sample, 73.0% of the subjects had been diagnosed previously with HT; in those who presented with AF, that figure was higher (92.1%).

We did not find, however, a relationship between higher BP levels and higher prevalence of AF, as might have been expected. On the contrary, both the lack of BP control and high systolic BP were associated with a lower prevalence of AF. In longitudinal studies of hypertense subjects, high BP (and high systolic BP in particular) is one of the most important factors associated with increased incidence of AF.^{26,27} Given that our study is a cross-sectional one with no follow-up, this inverse association in our study might be explained by more aggressive antihypertensive treatment in patients with AF: only 56% of treated hypertense subjects without AF received a combination of antihypertensive agents, whereas 76% of those with AF received combination therapy.

Only in the second model did we observe a weak association between the prevalence of AF and diabetes mellitus. This model included systolic and diastolic BP as continuous variables instead of diagnosis and control of BP as categorical variables. In the latter case, the relationship between AF and diabetes mellitus could be masked by the higher prevalence of HT in diabetic patients and poorer control of BP. Diabetes mellitus has been proposed as an independent risk factor for developing AF in some longitudinal studies.^{28,29} Changes in myocardial structure and function arising due to diabetes mellitus might favor the development of arrhythmia.³⁰ Evidence of LVH in the ECG, as well as greater cardiac mass in the echocardiographic examination, had already been reported as risk factors for developing AF.²⁶ Less clear is the association between abnormal renal function and AF. In our study, this association was significant even after adjusting for the other associated variables and deserves further study. Sex was not associated with AF in either of the models.

Several limitations should be taken into account in this study. First, although the study sample can be considered reasonably representative of the Spanish population for the age groups studied, we cannot be absolutely sure there were no selection biases. Although health coverage in Spain is universal, 28% of those invited to participate by telephone refused, and we do not have any information

[†]Model 2: includes the variables sex, age (5-year intervals), environment, smoking habit, sedentary lifestyle, systolic blood pressure, diastolic blood pressure, diabetes mellitus, left ventricular hypertrophy, renal function abnormality, and established cardiovascular disease.

on their profile. We cannot rule out that the subjects who refused to participate in the study had fewer risk factors and diseases, and so the prevalence of cardiovascular risk factors, cardiovascular disease, and even AF, might be slightly overestimated.

Second, the medical records did not reflect history of rheumatic valve disease. We do not know what impact this disease would have had on the multivariate analysis although the prevalence of this condition in the age range studied is very low. Third, the ECG readings were not taken in a centralized fashion. The investigators did, however, receive instructions on careful reading of the ECG given that the primary endpoint of the PREV-ICTUS study (estimating the risk of stroke) demanded an appropriate ECG reading for the detection of LVH and AF. Furthermore, ECG is a not particularly sensitive tool for diagnosing LVH, and we do not know what the findings of the study would have been, particularly from the point of view of associations in the multivariate analysis, had echocardiography been available. Fourth, BP was measured with an automatic monitor. There is little information of how accurate such monitors are in patients with AF, although some small studies have shown that at least some models can provide an appropriately accurate measurement in patients with AF³¹⁻³³ compared to mercury sphygmomanometry when several readings are taken. In our study, 2 readings were taken to determine the BP of the patient.

Finally, a satisfactory evaluation of cause and effect is not possible due to the cross-sectional nature of the study, and unexpected assocations can arise, such as better attainment of BP treatment goals being associated with higher prevalence of AF. Nevertheless, these limitations do not mean that the findings are not relevant, as this is the first study in Spain that has allowed an estimate of the prevalence of AF in older individuals in a reasonably representative sample of the Spanish population.

CONCLUSIONS

In conclusion, prevalence of AF in this reasonably representative sample of the Spanish population aged 60 years or over was 8.5%. This prevalence was stongly associated with older age, particularly age greater than 75 years, evidence of established cardiovascular disease, diagnosis of HT, and evidence of LVH in the ECG. The aging population and trends over time towards increased prevalence of AF suggest that more patients will suffer this type of arrhythmia in the future. Given the high rate of complications and mortality associated with AF, and given the lack of preventative measures clearly shown to reduce the incidence of AF, the health system in particular might benefit from well-designed trials to determine which primary prevention measures are effective in reducing the incidence of AF and its associated complications.

REFERENCES

- Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA. 2001;285:2370-5.
- Furberg CD, Psaty BM, Manolio TA, Gardin JM, Smith VE, Rautaharju PM. Prevalence of atrial fibrillation in elderly subjects (the Cardiovascular Health Study). Am J Cardiol. 1994;74:236-41.
- Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. Am J Cardiol. 1998;82:2N-9N.
- Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991;22:983-8.
- Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: the Framingham study. N Engl J Med. 1982;306:1018-22.
- Gajewski J, Singer RB. Mortality in an insured population with atrial fibrillation. JAMA. 1981;245:1540-4.
- Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation: 20year follow-up of the Renfrew/Paisley study. Am J Med. 2002; 113:359-64.
- Friberg J, Buch P, Scharling H, Gadsbphioll N, Jensen GB. Rising rates of hospital admissions for atrial fibrillation. Epidemiology. 2003;14:666-72.
- Candel FJ, Matesanz M, Cogolludo F, Candel I, Mora C, Bescos T, et al. Prevalencia de fibrilación auricular y factores relacionados en una población en el centro de Madrid. An Med Interna. 2004;21:477-82.
- Masiaa R, Sala J, Marrugat J, Pena A, Investigadores del Estudio REGICOR. Prevalencia de fibrilación auricular en la provincia de Girona: el Estudio REGICOR. Rev Esp Cardiol. 2001;54:1240.
- Labrador García MS, Merino Segovia R, Jiménez Domínguez C, García Salvador Y, Segura Fragoso A, Hernández Lanchas C. Prevalencia de fibrilación auricular en mayores de 65 años de una zona de salud. Aten Primaria. 2001;28:648-51.
- García-Acuña JM, González-Juanatey JR, Alegría Ezquerra E, González Maqueda I, Listerri JL. La fibrilación auricular permanente en las enfermedades cardiovasculares en España. Estudio CARDIOTENS 1999. Rev Esp Cardiol. 2002;55:943-52.
- Redón J, Cea-Calvo L, Lozano JV, Martí-Canales JC, Llisterri JL, Aznar J, et al. Blood pressure and estimated risk of stroke in the elderly population of Spain. The PREV-ICTUS Study. Stroke. 2007;38:1167-73.
- Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med. 2003;139:13747.
- 15. Casale PN, Devereux RB, Alonso DR, Campo E, Kligfield P. Improved sexspecific criteria of left ventricular hypertrophy for clinical and computer interpretation of electrocardiograms: validation with autopsy findings. Circulation. 1987;75:56572.
- Sokolow M, Lyon T. Ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads. Am Heart J. 1949;37:16186.
- Instituto Nacional de Estadística. Cifras de población [accesed 1 Jul 2006]. Available from: http://www.ine.es/inebase/cgi/um? M=%2Ft20%2Fe260&O=inebase&N=&L=
- Instituto de Demografía (1994), Proyección de la población española. Madrid, Instituto de Demografía/CSIC [accesed 1 Sept 2006]. Available from: http://www.ced.uab.es/publicacions/PapersPDF/ Text174.pdf.
- Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. Circulation. 2006;114:119-25.

- 20. Tsang TS, Petty GW, Barnes ME, O'Fallon WM, Bailey KR, Wiebers DO, et al. The prevalence of atrial fibrillation in incident stroke cases and matched population controls in Rochester, Minnesota: changes over three decades. J Am Coll Cardiol. 2003;42:93-100.
- Wolf PA, Benjamin EJ, Belanger AJ, Kannel WB, Levy D, D'Agostino RB. Secular trends in the prevalence of atrial fibrillation: The Framingham Study. Am Heart J. 1996;131:790-5.
- 22. Lake FR, Cullen KJ, De Klert NH, McCall MG, Rosman DL. Atrial fibrillation and mortality in an elderly population. Aust N Z J Med. 1989;19:321-6.
- Heeringa J, van der Kuip DA, Hofman A, Kors JA, van Herpen G, Stricker BH, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J. 2006;27:949-53.
- 24. Greenlee RT, Vidaillet H. Recent progress in the epidemiology of atrial fibrillation. Curr Opin Cardiol. 2005;20:7-14.
- 25. Healey JS, Connolly SJ. Atrial fibrillation: hypertension as a causative agent, risk factor for complications, and potential therapeutic target. Am J Cardiol. 2003;91(10A):9G-14G.
- Verdecchia P, Reboldi G, Gattobigio R, Bentivoglio M, Borgioni C, Angeli F, et al. Atrial fibrillation in hypertension: predictors and outcome. Hypertension. 2003;41:218-23.

- 27. Wachtell K, Lehto M, Gerdts E, Olsen MH, Hornestam B, Dahlof B, et al. Angiotensin II receptor blockade reduces new-onset 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.
- Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. JAMA. 1994;271:840-4.
- 29. Movahed MR, Hashemzadeh M, Jamal MM. Diabetes mellitus is a strong, independent risk for atrial fibrillation and flutter in addition to other cardiovascular disease. Int J Cardiol. 2005;105:315-8.
- Hayat SA, Patel B, Khattar RS, Malik RA. Diabetic cardiomyopathy: mechanisms, diagnosis and treatment. Clin Sci (Lond). 2004;107:539-57.
- Watson T, Lip GY. Blood pressure measurement in atrial fibrillation: goodbye mercury? J Hum Hypertens. 2006;20:638-40.
- Stewart MJ, Gough K, Padfield PL. The accuracy of automated blood pressure measuring devices in patients with controlled atrial fibrillation. J Hypertens. 1995;13:297-300.
- 33. Jani B, Bulpitt CJ, Rajkumar C. Blood pressure measurement in patients with rate controlled atrial fibrillation using mercury sphygmomanometer and Omron HEM-750CP deice in the clinic setting. J Hum Hypertens. 2006;20:543-5.