ARRHYTHMIAS

Permanent Atrial Fibrillation in Heart Disease in Spain. The CARDIOTENS Study 1999

José María García-Acuña^a, José Ramón González-Juanatey^a, Eduardo Alegría Ezquerra^b, Isidoro González Maqueda^c and José Luis Listerri^d

^aHospital Clínico Universitario de Santiago de Compostela. ^bClínica Universitaria de Navarra. Pamplona ^cHospital Universitario La Paz. Madrid. ^dUniversidad de Valencia. España.

Introduction and objective. Atrial fibrillation is the most common arrhythmia seen in clinical practice. The objective of this study was to know the frequency of atrial fibrillation and the characteristics of patients with atrial fibrillation in the Cardiotens study.

Material and method. A cross-section study with systematic selection of the study sample. All 32,051 outpatients seen on the same day by 1,159 physicians specialized in primary-care (79%) and cardiology (21%) were prospectively added to a database including history of cardiac disease (heart failure, coronary disease or atrial fibrillation), blood pressure, and ongoing treatment.

Results. Atrial fibrillation was present in 25% of patients with previous cardiovascular disease (6,194 patients), the prevalence being 4.8% (1,540/32,051) of the study population. Atrial fibrillation was more frequent in females 29%, (810/2,837) than in males, 22% (730/3,367), p < 0.005). Atrial fibrillation was present in 33% (469/1,420) of patients with heart failure and in 12% (387/3,226) of those with coronary heart disease. Arterial hypertension was diagnosed in 25% of the patients with atrial fibrillation. Only 33% of them were treated with oral anticoagulants (41% of the patients seen by cardiologists and 26% by primary-care physicians, p < 0.005). The antiarrhythmic drug most often used was digoxin (36%).

Conclusions. Atrial fibrillation had the same frequency and epidemiology in Spain as in other Western countries. Antithrombotic therapy is underused by primary-care physicians and cardiologists.

Key words: *Hypertension. Atrial fibrillation. Anticoagulants.*

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The CARDIOTENS study was undertaken by the Seccion de Hipertension de la Sociedad Española de Cardiología (the Hypertension Section of the Spanish Society of Cardiology) and the Sociedad Española de Medicine Rural y Generalista (Spanish Society of Rural and General Medicine).

Correspondence: Dr. J.M. García Acuña. Avenida da Mahía , 106, P-1, 3.° C. Bertamirans-Ames. 15220 A Coruña. España. E-mail: jgarciaacuna@meditex.es

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La fibrilación auricular permanente en las enfermedades cardiovasculares en España. Estudio CARDIOTENS 1999

Introducción y objetivo. La fibrilación auricular (FA) es la arritmia más frecuente en nuestro medio y uno de los factores de riesgo más importante para desarrollar un ictus. El objetivo es conocer la frecuencia de la FA, así como sus características clínicas y su tratamiento, en una muestra de 32.051 pacientes atendidos en la consulta de cardiología y de atención primaria.

Material y método. Se trata de un estudio transversal con selección sistemática de la muestra del estudio. Se registraron de forma prospectiva en un cuestionario uniformizado los datos demográficos, clínicos, tensionales y terapéuticos de todos los pacientes atendidos en un mismo día por 1.159 médicos (21% cardiólogos y 79% de atención primaria).

Resultados. La FA estaba presente en el 25% de los pacientes con enfermedades cardiovasculares (6.194), lo que representa una prevalencia del 4,8% (1.540/32.051). La FA fue significativamente más frecuente en las mujeres (29%, 810/2.837) que en los varones (22%, 730/3.367; p < 0,005). El 33% (469/1.420) de los pacientes con insuficiencia cardíaca y el 12% (387/3.226) de los portadores de cardiopatía isquémica presentaban esta arritmia. El 25% de los pacientes con hipertensión arterial estaba en FA. Sólo el 33% de los enfermos en FA recibía tratamiento anticoagulante (41% del cardiólogo frente al 26% del generalista, p < 0,005). El antiarrítmico empleado con mayor frecuencia fue la digoxina (36%).

Conclusiones. La FA presenta una frecuencia y una distribución por edad similares a las encontradas en estudios realizados en otros países de nuestro medio. El empleo de anticoagulantes es subóptimo tanto en la consulta especializada como en la de atención primaria.

Palabras clave: Hipertensión arterial. Fibrilación auricular. Anticoagulantes.

ABBREVIATIONS

AF: atrial fibrillation. HCTZ: hydrochlorothiazide. AHT: arterial hypertension. CI: cardiac insufficiency. DAP: diastolic arterial pressure. SAP: systolic arterial pressure

INTRODUCTION

Atrial fibrillation (AF) is the most frequent disturbance of rhythm found in the population. Its frequency increases with advancing age.¹ The majority of epidemiological data on AF come from the Framingham study;² nevertheless, studies that analyze the prevalence and incidence of AF are very limited. In addition, it is suspected that its true prevalence is underestimated.^{3,4}

Five large studies⁵⁻⁹ have shown the benefit of anticoagulant treatment in the prevention of thromboembolic phenomenon in patients with AF who do not have rheumatic valve disease. These studies have demonstrated the existence of a series of groups who are particularly high risk.

Nevertheless, despite the importance of these therapeutic considerations, the administration of anticoagulant treatment continues to be less than optimal and, according to estimates, its use could avoid 31 ictus for every 1000 patients treated during 1 year at the cost of 1 major hemorrhage and 50 lesser hemorrhagic episodes.¹⁰

The 1999 CARDIOTENS study, undertaken cojointly by the Sección de Hipertensión de la Sociedad Española de Cardiología (Hypertension Section of the Spanish Society of Cardiology) and the Sociedad Española de Medicina Rural y Generalista (Spanish Society of Rural and General Medicine), was designed with the objective of understanding heart disease in clinical practice in Spain. Our study presents the principal characteristics of AF that were included in the 1999 CARDIOTENS study.

MATERIALS AND METHODS

The 1999 CARDIOTENS study was designed by the Sección de Hipertensión de la Sociedad Española de Cardiología (SEC-HTA) and the Sociedad Española de Medicina Rural y Generalista (SEMER-GEN). The study was carried out by 1159 physicians (21% were cardiologists and 79% were primary care physicians) throughout Spain with representatives from all geographical areas of members of SEC-HTA

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and SEMERGEN. These physicians agreed to participate in the study by responding affirmatively to a letter sent to all physicians who belong to both societies. All filled out a previously designed questionnaire that requested all the characteristics of patients who came to their outpatient clinics during 1 single day between the months of June and September, 1999. Therefore, this was a transverse study with systematic selection of the study sample.

Data collection

Permission was requested from all patients who received treatment in the outpatient clinic from physicians during the day chosen to include their data in the database. No patient refused to be included in the study.

Data was collected by means of a questionnaire designed for this purpose, and the data was later entered into a database. The data included the characteristics of the physician who participated in the study (age, sex, place of employment, geographic area) along with patient demographic data, cardiovascular risk factors (CVRF), cardiovascular pathology, previous clinical history, and treatment received by the patient.

The questionnaire that the participating physicians completed was made up of 2 parts. The first part concerned the patient's age, sex, existence of CVRF, previous cardiovascular pathology, and treatment the patient was receiving.

A patient was considered hypertensive if this was a diagnosis made previously or when the patient was receiving treatment for hypertension. Clinical heart disease was considered to be cardiac insufficiency (CI) diagnosed by the usual criteria,¹¹ ischemic heart disease evident by a previous history of myocardial infarction or chest pain, cardiac rhythm disturbance, concrete chronic AF documented by electrocardiography recordings (cases of paroxysmal AF, whether persistent or isolated, were not registered), left ventricular hypertrophy observed on ECG or echocardiography study, and, lastly, significant valve disease.

Only those patients who presented with a history of heart disease or with CVRF completed the second part of the questionnaire. The second part concerned the tension level, plasma lipid values, and the details of the treatment these patients received.

Arterial pressure (AP) that was measured for the patients included in this study was determined on the same day that the questionnaire was filled out (casual pressure). The measurement was performed according to the recommended guidelines.

The qualitative values analyzed in this study were arterial hypertension (AHT), diabetes, dyslipemia, smoking, and obesity. The quantitative variables studied that allowed the patients to be grouped into ranges were systolic arterial pressure (SAP) and diastolic arte-

Age (years)	Primary care	Specialized care	Total
<50	0.44% (46/10 778)	7.92% (70/883)	0.99% (116/11 661)
50-59	2.03% (84/4145)	13.71% (109/795)	3.90% (193/4,940)
60-69	3.41% (198/5804)	20% (250/1280)	6.32% (448/7084)
70-79	5.51% (274/4974)	22.18% (256/1104)	8.71% (530/6078)
>79	8.26% (160/1935)	26.34% (93/353)	11.05% (253/2288)
Sex			· · · · · · · · · · · · · · · · · · ·
Women/Men	2.94%/2.49%	18.75%/16.65%	5.53%/4.11%
Total	2.75% (762/27 636)	17.62% (778/4415)	4.80% (1540/32 051)

TABLE 1	Prevalence	of AF	in different	age	groups
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The denominator corresponds to the number of patients seen in each age group in specialty and primary care practices.

rial pressure (DAP). The patients were grouped according to 3 ranges: SAP>140 mm Hg, SAP between 131 mm Hg and 139 mm Hg, or SAP<130 mm Hg; the ranges established for DAP were >90 mm Hg, between 81 mm Hg and 89 mm Hg, and <80 mm Hg. In addition to the questionnaire, the physicians were asked if the patient's arterial pressure was under control (in accordance with the accepted current recommendations, which are SAP<140 and DAP<90 mm Hg).

Statistical analysis

Once all the questionnaires had been received, the information was validated and entered into the database built for this purpose, via the Star program, version 17.

The numerical variables were presented as mean± standard deviation (SD), and their correlation was analyzed by Student *t* test. The non-quantitative variables were described in terms of their absolute and relative frequency in percentages, and were analyzed via the c2 test. The range groups were analyzed by bivariate correlation study using the c2 test. The association between 2 dichotomous variables was analyzed by means of the c2 test with Yates correction or the exact Fisher test, as appropriate. In all cases it was established that the significance level of the alpha error at which the null hypothesis was rejected was P=.05.

RESULTS

In the 1999 CARDIOTENS study 32,051 patients

were included, of which 27 636 (79%) were seen by primary care physicians and 4415 (21%) by cardiologists participating in the study. The mean and average of patients studied by primary care physicians was 30 and 24, respectively, and 18 and 15, respectively, for the cardiologists.

Prevalence, sex, and age

There was a history of heart disease in 6 194 patients (19%); 25% had a diagnosis of AF, or a prevalence of 4.8% (1540 patients) of the total number of patients included in the study. This group of patients was significantly larger for the cardiology practices than the primary care practices (28% versus 23%, respectively; P < .05). Table 1 reflects the prevalence of AF with regard to age and gender; AF was more prevalent in all older groups seen in the specialized practices. The great majority of patients were more than 60 years of age and only 20% were younger than 60 years of age. Patients of between 70 and 79 years of age made up more than 40% of the total number of patients with AF, followed by the group of patients between the age of 60 and 69 years, or approximately 30% (Figure 1).

Table 2 shows the percentage of patients in AF as a function of sex and age seen both by specialists and primary care physicians; specialists saw more women and patients of a greater age. AF was significantly more prevalent in women than in men (29% vs 22%; P<.05) (Figure 2). These data mean that the prevalence of AF in the sample analyzed was 5.5% in women vs 4.1% in men.

TABLE 2. The presence of AF in patients with cardiovascular disease seen by primary care physicians and by specialists according to sex

	Primary care		Spec	Total	
	Women	Men	Women	Men	Total
Sex Mean age, years	480/762 (63%) 71±10.2	282/762 (37%) 69.2±9.5	381/778 (49%) 68.3±12.7	397/778 (51%) 64.7±8.9	1540 68.4±10.3



Fig. 1. Presentation by age groups of patients with atrial fibrillation seen both by specialists and primary care physicians. **P<.05.



Fig. 2. Distribution of sex differences in patients with a history of cardiovascular disease from the study sample of the 1999 CARDIOTENS study. Women presented with AF more frequently than men. ***P*<.05.

Atrial fibrillation and risk factors

AHT was found in 10,555 patients (33%) in the study sample. AF presented with a similar frequency in both patients with hypertension and patients with diabetes with a cardiovascular history (25% of patients). Nevertheless, when patients presented with dyslipemia and cardiovascular disturbances, the prevalence was significantly less than in the previous risk groups (17% of patients).

There were a total of 999 patients with hypertension who had AF, of which 70% were more than 70 years of age, constituting the most important group of statistical significance (P<.05) in the primary care practices, while patients of less than 60 years of age formed the most numerous group seen by specialists (P<.05). Nevertheless, 60% of patients with AF presented with hypertension.

Cardiovascular diseases

Nineteen percent (32 051 patients) of the sample analyzed presented with cardiovascular disease (Figure 3).

AF was the most frequently seen arrhythmia in those patients with a history of cardiovascular disease (61%), both in the specialist practices and in the pri-



Fig. 3.Distribution of the different cardiovascular antecedents in the sample studies, as seen by the cardiologist or the primary care physician. Note the greater percentage of patients with AF seen by the cardiologist. ***P*<.05.





mary care practices (P=ns) (Figure 4).

Table 3 shows the prevalence of AF in patients with cardiovascular disease.

In the group of patients with CI, AF was present in

33% of cases, being the arrhythmia that was seen more frequently in patients seen by cardiologists (40%) than patients seen by primary care physicians (29%) (P<.05). In this group of patients a greater prevalence

TABLE 3. Prevalence of AF in patients with cardiovascular disturbances according to whether they were seen by primary care physicians or cardiologists

	Primary care (n=3363)	Cardiologists (n=2831)
Cardiac insufficiency	9.51% (320)	10.80% (306)
Ischemic heart disease	9.12% (307)	10.38% (294)
Angina	4.75% (160)	6.25% (177)
Infarct	4.37 % (147)	4.13% (117)
Valve disease	5.14% (173)	10.80% (306)

of AF was also observed in women than in men (37% vs 30%, respectively; P < .0001), and this increased to 47% for patients with CI who were seen by specialists.

AF was found in 12% of patients with ischemic heart disease, with a higher prevalence rate in those patients seen by cardiologists than those seen by primary care physicians. As in previous groups, there was a slight but significant difference between the sexes in favor of women (14% vs 11%; P<.05).

Atrial fibrillation and treatment

Figure 5 shows the medications that the patients with AF received. What stands out in the therapeutic management of patients with AF was that digitalis was the anti-arrhythmia drug most frequently used (36% of cases), while other anti-arrhythmia drugs such as midiron, quinidine, flecainide, and propafenone were administered in 35% of patients. Beta-blockers and calcium antagonists were only used in 14% and 21% of patients with AF, respectively.

When we compared the medications received by patients seen by primary care physicians and by cardiologists, we observed that digitalis and the anti-arrhythmia agents were employed more frequently by the latter. The primary care physicians prescribed insulin, angiotensin enzyme conversion inhibitors (AECI), and hydrochlorothiazide with more frequency than the specialists.

Only 28% of patients with AF took anticoagulants and 31% received antiaggregate medication. Treatment by the specialists was characterized by greater use of oral anticoagulants (37% vs 21%; P<.001) and antiarrhythmia agents (37% vs 33%; P<.001). The specialists used beta-blockers more commonly than the primary care physicians (18% vs 10%; P<.001), which can be observed from the data shown in Figures 5 and 6.

Only 33% of patients with hypertension received chronic anticoagulation therapy; use of this treatment was more common in cardiology practices (41% vs 26%; P<.05), and it was also observed that the younger hypertensive patients received anticoagulants more frequently than patients of advanced age (Tables 4 and 5).

DISCUSSION

AF is the arrhythmia most frequently encountered in daily clinical practice. There are no epidemiological studies in our field that have analyzed the situation with AF. Our analysis of the CARDIOTENS study of this subgroup of patients aims to provide data in this regard. AF represents 25% of the cardiovascular antecedents of the patients included in our study.

Prevalence and influence of age in patients with AF

The impact of AF in the general population of wes-



Fig. 5. Presentation of the medications received by the general population of patients with AF.



Fig. 6. Differences in the pharmacological treatment of patients with AF according to the treating physician.

tern countries has been progressively increasing with the aging of the population.¹² Data from the National Ambulatory Medical Care Surveys showed that the number of hospital admissions for AF tripled between 1980 and 1992, and this same study found that the diagnosis of AF increased between 1982 and 1993 from 30.6% to 59.6% per 10 000 inhabitants.¹³ The 1999 CARDIOTENS study included a total of 32 501 patients, of which 6194 had a history of cardiovascular disturbances (19.05%), 25% of which presented with AF, or a prevalence of 4.76% of the sample analyzed. The prevalence rate by sex was significantly greater in women (5.5%) than in men (4.1%) (*P*<.05). This difference is probably a result of the greater longevity of women. Similar data was also found in other study populations,¹⁴ suggesting the methodological validity of our study design.

The 1999 CARDIOTENS study points out that the majority of patients were more than 60 years of age, with the group of age 70 to 79 years being the largest with more than 40% of patients, and among these the prevalence of AF was the highest of the total sample. The data obtained from the specialist practices could not be considered valid because the sample was skewed; nevertheless, our overall analysis is similar to the results that have been published by other studies.¹²⁻¹⁶

Atrial fibrillation and cardiac insufficiency

TABLE 4. Distribution by percentages of anticoagulation and aggregation treatment rates by age of patients with hypertension and AF

	Total (n=999)	< 69 years of age (n=396)	70-79 years of age (n=391)	>79 years of age (n=212)	PC (n=532)	PC cardiology (n=467)
Standard deviation	9.89	3.01	2.8	3.42	9.64	9.79
Ischemic heart disease	26%	26%	27%	23%	25%	27%
Antiaggregants	39%	32%	42%	47%	39%	39%
Anticoagulants	33%	39%	32%	24%*	26%	41%*

**P*<.05

	PC			Cardiology		
	<65 years of age (n=89)	65-80 years of age (n=314)	>80 years of age (n=129)	<65 years of age (n=132)	65-80 years of age (n=277)	>80 years of age (n=58)
Standard deviation	6.31	4.55	3.32	5.94	4.31	3.19
Ischemic heart disease	32%	25%	20%	21%	28%	33%
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Antiaggregants	36%	39%	43%	24%	42%	55%
				†	*	
Anticoagulants	27%	28%	19%	50%	40%	26%
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TABLE 5. Distribution by percentages of anticoagulat	tion and aggregation treatment rates by age of	patients
with hypertension and AF according to whether they	were seen by a cardiologist or a primary care	physician

***P*<.05

Congestive CI is a serious cardiovascular condition that can be worsened by factors that are not directly related to ventricular dysfunction. AF in this group of patients causes a lower tolerance for physical exercise, worsening of NYHA functional class, and thromoembolic complications. It has been observed that many patients with AF with a rapid ventricular response present with CI and serious depression of left ventricular systolic function that resolves when the sinus rhythm is restored, although the frequency of this finding is not clear.^{17,18}

The 1999 CARDIOTENS study underlines the fact that AF is present in 33% of patients with CI, a number that is slightly higher than that found in multicenter studies of CI. In the DIAMOND study,¹⁹ AF was present in 25% of patients in the group that received an active medication (dofetilide) and in 27% of patients assigned randomly to a placebo.²⁰⁻²²

Given the characteristics of our study it is not possible to know the prognostic effect of AF in this group of patients. Various studies have found an increase in the mortality rate in patients with CI and AF.²³⁻²⁵

Atrial fibrillation and ischemic heart disease

Angina is a common symptom during episodes of AF; nevertheless, the prevalence of AF among patients with coronary lesions as revealed by coronary angiography is low, varying between 0.2% and 5%.²⁶ The CASS (Coronary Artery Surgery Study) study²⁷ found only a 0.6% prevalence rate of sustained AF in more than 18 000 patients who presented with cardiac catheterization. This arrhythmia was significantly associated with older patients, with CI and mitral regurgitation. Certain studies^{2,28,29} showed that age and CI, dysfunction of the papillary muscle, and the presence of an atrial infarct increased the risk of the patient developing AF.

In the 1999 CARDIOTENS study it was observed that ischemic heart disease was present in 10% of the patients included in the study, and this was the cardiovascular antecedent seen most frequently (in 51% of patients). AF was present in 12% of patients who had chronic ischemic heart disease. The sample analyzed in our study was very heterogeneous and comparisons could not be established with other records, such as CASS, in order to find out the prevalence of AF in this group.

Given our study parameters, it was not possible to determine the prognostic effect of AF in this group of patients. Various studies have indicated an increase in the mortality rate in patients with CI and AF.²³⁻²⁵

Atrial fibrillation and ischemic heart disease

Angina is a common symptom during episodes of AF; nevertheless, the prevalence of AF in patients with coronary lesions shown on coronary angiography is low, and varies from 0.2% to 5%.²⁶ The CASS study (Coronary Artery Surgery Study) found only a 0.6% prevelance of sustained AF in more than 18 000 patients who underwent cardiac catheterization. This arrhythmia is significantly associated with older patients, with CI and mitral regurgitation. Certain studies^{2,28,29} have shown that age and CI, papillary muscle dysfunction, and atrial infarct increase the risk of developing AF.

In the 1999 CARDIOTENS study, it was observed that ischemic heart disease was present in 10% of the patients included in this study and that this was the cardiovascular antecedent that was found most frequently (51%). AF was present in 12% of patients who

had chronic ischemic heart disease. The sample analyzed in our study is heterogeneous and thus cannot be compated with other studies, such as CASS, in order to establish the prevalence of AF in this group.

Atrial fibrillation and arterial hypertension

There are few published studies that, from an epidemiological point of view, examine the relationship between AHT and AF. Recently, studies have been published regarding the impact of hypertension on heart disease,³⁰ and it has been observed that 66% of patients diagnosed with chronic AF have a history of AHT. An interesting finding was the low rate of patients receiving anticoagulant treatment (25%) in a clinical situation that was characterized by a high frequency of thromboembolic phenomena.^{4-7,31}

In the Framingham study, it was observed that AHT and left ventricular hypertrophy present on ECG increased by up to a factor of 4 the risk of developing AF (adjusted for age).^{22,32} In the analysis of the subgroup of patients with AF and systemic AHT in the 1999 CARDIOTENS study, it was shown that there was a greater presence of AF in women, probably due to the fact that women tend to live longer.

Atrial fibrillation and diabetes mellitus

Few studies exist regarding the relationship between AF and diabetes mellitus; nevertheless, this relationship is shown in the Framingham study, where diabetes is considered responsible for increasing the risk of AF up to 2 times for both men and women. This clinical condition has a slight relationship to obesity. Most likely diabetes favors this situation because it coexists with other cardiovascular conditions, such as ischemic heart disease, CI, and AHT.^{14,22,32,33} In our study we found 1275 patients with diabetes who had a history of cardiovascular disturbances, of which 60% presented with ischemic heart disease; 27% with CI, and 25% with AF.

Atrial fibrillation and anticoagulation

Many epidemiological studies have pointed out that AF constitutes an independent risk factor for the occurrence of an ictus.³⁴⁻³⁷ AF was responsible for nearly 25% of ictus that occurred in subjects between 80 and 89 years of age in the Framingham study.³⁸ The annual incidence of ictus is similar in both patients with intermittent AF and sustained AF.³⁹

Five studies⁵⁻⁹ have shown during an average follow-up period of 1.2 to 2.3 years that there was a 68% reduction in the risk of suffering an ictus in patients with AF who received chronic anticoagulant therapy, without a significant increase in the risk of hemorrhage. García-Acuña JM, et al. Atrial Fibrillation in the 1999 CARDIOTENS Study

The only study of secondary prevention was the European Atrial Fibrillation Trial (EAFT), which showed a 60% reduction in the risk of recurrent ictus.⁴⁰

It has also been confirmed that AF is responsible for cerebrovascular accidents, especially in patients of advanced age, who are hypertensive, or who are overweight.⁴¹

Our findings show a low rate of anticoagulation therapy in the population of patients with AF (39%), especially in the primary care setting. Even when hypertensive patients are examined in AF (a particularly embologenic condition), only 33% of these patients received chronic anticoagulant therapy. The patients who most often were treated with anticoagulants were less than 69 years of age (39%), while those who were older than 70 years of age did not surpass 35%. Similar results were found in a retrospective study.⁴²

Study limitations

This was an observational, transverse, study with the purpose of finding out what the situation was with regard to patients with permanent AF who were treated in a primary care or a specialist practice. The study design is not adequate for documenting the actual prevalence of AF in Spain, but it represents an approximation, probably quite accurate, of reality. Cases of isolated, persistent, or paroxysmal AF were not recorded, which also limits the estimate of AF prevalence.

We could not extract prospective conclusions from our data as the fact that the study was an open study may cause somewhat of a skew with regard to patient selection.

CONCLUSIONS

With the data obtained in this study we can state that AF is present at a rate that is similar to that observed in other epidemiological studies performed in similar circumstances to ours, in which women present with this arrhythmia with more frequency than men, probably due to their greater longevity.

CI, AHT, and ischemic heart disease are frequently associated with AF.

Anticoagulant treatment is under-utilized in general by both primary care physicians and cardiologists. Older age groups with risk factors are those most affected by the under-use of anticoagulation therapy.

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