Diagnosed, undiagnosed and overall atrial fibrillation research on population over 60 year-old. AFABE study

Josep Luís Clua-Espuny1, Ramon Bosch-Princep2, Albert Roso-Llorach3, Carlos López-Pablo4*, Emmanuel Giménez-Garcia5, Núria González-Rojas6, Jorgina Lucas-Noll1, Anna Panisello-Tafalla1, Iñigo Lechuga-Duran7 and Miquel Gallofré-Lopez8

*Correspondence: clpclp3@gmail.com

1ABS Tortosa-Est Primary Care, Family and Community Specialist, Catalan Institute of Health, Regional Management Terres de l’Ebre, CAP Temple, Place carrilet,Tortosa-Spain.
2Department of Research, ICS Terres de l’Ebre, Hospital de Tortosa Verge de la Cinta, Tarragona, Spain.
3IDIAP Institute for Research in Primary Care (IDIAP) Barcelona, Spain.
4Department of Molecular Biology and Research, Tortosa Verge Cinta Hospital, IDIAP Institute for Research in Primary Care, IISPV and URV, Spain.
5Antares Consulting HEOR, Barcelona, Spain.
6Health Economics, Boehringer-Ingelheim España, Sant Cugat del Vallès, Barcelona, Spain.
7Department of Cardiology, Tortosa Verge Cinta Hospital, Tortosa Verge Cinta Hospital, Tarragona, Spain.
8Director of Catalonia Cerebral Vascular Disease, Health Department of the Government of Catalonia, Barcelona, Spain.

Abstract

Background: Undiagnosed atrial fibrillation usually is only detected with the first complication. We estimated undiagnosed Atrial Fibrillation prevalence, overall AF and associated factors in a public health-service area in Catalonia, north-eastern Spain.

Methods: Multicentre, cross-sectional study, with people randomly selected among the attended population over 60 years old by primary care teams regardless of follow-up time in health centres or at homes. Information was collected through ECGs, electronic medical history reviews and medical interviews. Descriptive and logistic regression analysis was performed.

Results: 1043 subjects were recruited (47.1% male), mean age: 73.1 y-o (SD: 7.8 y-o); 43.3% ≥75-year-old. Overall AF prevalence was 10.9% (CI95% 9.1-12.8%); higher in men than in women, progressively increasing with age (24.4% in ≥85-year-old). Only women ≥85-year-old had higher prevalence (26.2%) than men (22.5%). Undiagnosed AF relative prevalence was 2.2% (IC95% 1.3-3.1%). These results show that about 1 in 50 people over 60 years old could suffer undiagnosed AF. The higher risk of AF undiagnosed was found in: men (OR 2.5 IC95% 1.0-6.2), >75 years old (OR 2.5 IC95% 1.0-6.1), heart failure history (OR 5.2 IC95% 1.3-20.9), who live in rural areas (OR 15.9 IC95% 1.5-160.1) and to whom no one ECG was performed in the last two years.

Conclusions: The overall AF prevalence increased 10 times from the sixties to over eighties and the proportion man-woman changes from 4:1 to 1:1. The undiagnosed AF prevalence was 2.2% (IC95% 1.3-3.1). This percentage should be added to the one of untreated cases with OAC.

Keywords: Atrial fibrillation, prevalence, elderly people, diagnosed, undiagnosed, primary care

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice [1] that affects 1-2% of general population although estimates and projections of diagnosed prevalence of AF have been highly inconsistent across published studies. The life-time risk to develop AF increases with the age and it is higher in man than in women [2]. Due to the ageing population and the increasing prevalence of the known risk factors for AF, the number of patients with AF is expected to be the triple in the next four decades as well as its complications, like stroke [3-6]. In addition, the cost of managing AF patients and its complications have been well documented to be high [7]. This will have serious implications for the planning of health and welfare systems, especially not only because of these predictions of AF prevalence continuous increase [3,8,9] but also because the current cost containment economical context. Furthermore, the paroxysmal nature of AF at onset [10] makes difficult to establish the overall AF prevalence and it is still probably underestimated systematically [11] with a percentage ranging from 0.5-1.7% [12-15]. It has also been demonstrated to be an important cause of the cryptogenic stroke [16,17]. An early diagnosis and a treatment are essential to reduce the rate of morbidity and mortality.

The aim of this study was to estimate undiagnosed AF prevalence and the associated risk factors in the population over the sixties who were attended by primary care teams in a public health-service area in Catalonia, north-eastern Spain.

Methods

AFABE study is a cross-sectional, multicentre study (22 primary
considered clinical conditions were defined in the patient dataset coded using the ICD-10 classification.

The income per capita is significantly lower (93.7%) from the Catalonia average. Demographically speaking, in the last two decades the gross tax about the total demographic growth is characterized by the natural negative growth, the higher ageing factor and the quickly increase from 2000(12.36/1000 inhab.) to 2006 (26/1000 inhab.) caused by migratory movements which meant a 14.71% from the actual population. The population over the eighties in the period 1986-2006 has increased its proportion in about a 66% taking a 3.5% to 5.9% from the total population, without changes between man- woman, but meaning a 60% of women in the population over 80 years old.

Taking into account the inhabitants of the area (N 82,000), the population over the sixties (n 20733), the estimated AF prevalence for Spanish inhabitants (8.5%) [15] and under the hypothesis of a 34% of non-diagnosis [1], 600 patients in Baix Ebre area should remained undiagnosed (2.9% of people over 60-year-old). The sample necessary to analyze for the percentage of undiagnosed patients were 1.029, considering IC95%, 1% precision error and 2.9% hypothesis of undiagnosed AF prevalence. It included a 10% of people who were attended at their homes or at nursing or care or old people’s homes.

The health centres were classified as rural if they were located in towns with <1,000 inhabitants, Semi-urban between 1,000 and 10,000, and Urban >10,000. The territory is formed by a low density of population in comparison to the Catalan average, with a tax about a 53.6 inhabitants/km2 significantly lower than the Catalan average that is about 212 inhabitants/km2. A 46.1% of inhabitants live in big towns, the 16.4% in towns with less than 1000 and the rest of them is divided into medium towns.

A patient was considered positive to AF when it could be demonstrated that he or she has or have had at least an AF positive 12-lead ECG [1]. Every patient who presented with AF for the first time was considered a patient with first diagnosed AF and after 8 days of this ECG, a new follow up was done to be classified as persistent or paroxysmal AF [1].

Studied patients could be placed in four groups: 1) Patients always negative for AF; 2) Patients with a current positive ECG and previously diagnosed AF (ICD-10 I48); 3) Patients with a current negative ECG and previously diagnosed AF (ICD-10 I48); and 4) Patients with a current positive ECG but previously negative or unknown (previously undiagnosed patients or newly diagnosed patients). We excluded the patients ≤60 years old, without electronic medical history (the individual clinical register was not used at least once in the last three years), and those patients who didn’t give their consent.

Different types of AF prevalence (Figure 2) were considered in this article:

1. Overall AF prevalence: percentage of people with at least one documented AF ECG. The patient could be diagnosed at the moment of the study or previously (patients of groups 2, 3 and 4).
2. Previously diagnosed AF prevalence: percentage of patients with a documented AF diagnosis history (patient dataset coded with I48). It was divided in two subgroups: a) previously diagnosed AF with current positive ECG prevalence: prevalence of patients at group 2. b) previously diagnosed AF with current negative ECG prevalence: prevalence of patients at group 3.
3. Undiagnosed AF prevalence: percentage of subjects newly diagnosed of AF during this study (patients of
group 4) Current AF prevalence: percentage of people with an ECG positive for AF at the moment of performing this study (groups 2 and 4 patients) independently of their previous diagnosis status.

![Figure 2. Distribution of the studied subjects and atrial fibrillation prevalences.](image)

N: number of cases; AF: Atrial fibrillation; ECG: Electrocardiogram negativity for AF; E ECG+: electrocardiogram positivity for AF; c+AF: AF with current positive ECG; uAF: previously undiagnosed AF; dAF: previously diagnosed AF; c+dAF: previously diagnosed c+AF; c-dAF: previously diagnosed with current ECG -; oAF: overall AF.

**Statistical analysis**

In the descriptive analysis, data for categorical variables are expressed as number of cases and percentage and, data for continuous variables are expressed as a mean with its standard deviation. Categorical variables were compared using a χ² test or Fisher's exact test as required. Continuous variables were compared using Student's test or Mann-Whitney test depending on the normal distribution assumption. Normal distribution was checked by the Shapiro-Wilk test. A logistic regression analysis was performed to find possible risk factors that characterize the population with undiagnosed AF. Factors that were independently associated in the one way analysis, being at least marginally significant (p≤0.1) were included using a backward step-wise strategy. A p-value of less than 0.05 was considered to indicate statistical significance. The analysis was carried out with the SPSS statistical software package (version 19).

**Results**

1043 people were included in the study. Their average age was 73.1 years old (SD: 7.8), and 52.9% were women. Relevant clinical data related with cardiovascular risk factor are shown in (Table 1). High prevalence of some CVRF was found: hypertension (66.0%), diabetes mellitus type 2 (27.0%), and myocardial infarction (8.4%). Three quarters (76.6%) of the studied population had undergone at least an ECG in the last two years. There were not statistical differences between rural and non-rural populations in demographic and CVRF prevalence. By contrast, there were observed important differences in the prevalence of these CVRF by gender. Men had significantly more prevalence of DM2, previous stroke, vascular diseases and smoking and in contrast women had been less studied with ECG.

After the ECG performing (Figure 2) 87 (8.3%) subjects showed an AF positive ECG at the moment of the study. 64 (73.5%) of these 87 had a previously diagnosed AF and 23 (26.4%) had a previously undiagnosed AF. Regarding the 956 (91.6%) subjects without AF at the moment of study, 27 (2.8%) subjects had an AF which has been previously registered in their medical history. So, the sum of previously diagnosed AF was at the moment of the study 91 cases.

The distribution of the AF cases after the ECG recording and the prevalence of the different types of AF are illustrated in (Figure 3). The average time from the AF diagnosis was 5.22 years (SD: 3.66). The overall AF prevalence was 10.9% (IC95% 9.1-12.8) and when it was stratified by gender and age (Figure 3) groups progressively increased from 2.4% to 24.4% in patients over 85 years; and men had higher prevalence than women in all age groups except for the group of over 85-year-old patients in which women reached the highest prevalence detected in this study (26.2%).

The distribution of the different subtypes of AF by age groups can be appreciated in (Figure 4). Patients from 61 to 69 years had similar low prevalence of the different types of AF that ranged from 0.6% to 1.3%. Important increases of overall AF prevalence occurred in individuals over 70 years old which increased progressively from 1.4 times for the group of people 65-69 years old, 4.5 times) for 70-74, 5.88 times for 75-79, 8.1 times for 80-84 and 10.21 times for ≥85 years old. This huge increase is mainly produced in the prevalence of the previously diagnosed AF (28.5 times) with current positive ECG. We found the main concentration of previously diagnosed AF without current confirmatory in the age groups of 70-74 and 75-79 years old (3.0 times).

The undiagnosed AF prevalence investigated with single ECG recordings for people over the sixties was 2.2% (IC95% 1.3-3.1). These results show that about 1 in 50 people over 60 years old could suffer undiagnosed AF. Although it showed an irregular age distribution ranging from 7% to 37% of the overall AF prevalence, it increased 6.1 times at the end of the study and represented the 26.4% (IC95% 18.3-36.6%) of the all AF detected in the ECG performed specifically for this study and the 20.2% (IC95% 13.8-28.5%) of the overall AF (Figure 2). After 8 days of follow up, 74% of undiagnosed AF cases were classified as persistent AF, 14% as paroxysmal AF and 12% were lost of follow up; when cases lost of follow up were excluded,
Table 1. Study subjects characteristics’ and cardiovascular risk factors prevalence by gender and living area.

<table>
<thead>
<tr>
<th>Variables</th>
<th>All</th>
<th>Rural</th>
<th>Non-Rural</th>
<th>Men</th>
<th>Women</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Num. of cases (%)</td>
<td>Num. of cases (%)</td>
<td>Num. of cases (%)</td>
<td>P-value</td>
<td>Num. of cases (%)</td>
<td>Num. of cases (%)</td>
<td>P-value</td>
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<tr>
<td><strong>Gender</strong></td>
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<tr>
<td>Men</td>
<td>491 (47.1)</td>
<td>80 (46.8)</td>
<td>411 (47.1)</td>
<td>0.93</td>
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<td>Women</td>
<td>552 (52.9)</td>
<td>91 (53.2)</td>
<td>461 (52.9)</td>
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<tr>
<td><strong>Age (≥75)</strong></td>
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<td></td>
<td>452 (43.3)</td>
<td>81 (47.4)</td>
<td>371 (42.5)</td>
<td>0.25</td>
<td>222 (45.2)</td>
<td>230 (41.7)</td>
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<tr>
<td><strong>Hyper tension</strong></td>
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<td></td>
<td>688 (66.0)</td>
<td>112 (65.5)</td>
<td>576 (66.1)</td>
<td>0.89</td>
<td>331 (67.4)</td>
<td>357 (64.7)</td>
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<tr>
<td><strong>Diabetes Mellitus</strong></td>
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<td></td>
<td>282 (27.0)</td>
<td>51 (29.8)</td>
<td>231 (26.5)</td>
<td>0.37</td>
<td>150 (30.5)</td>
<td>132 (23.9)</td>
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<td><strong>Cardiac failure</strong></td>
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<td></td>
<td>44 (4.2)</td>
<td>6 (3.5)</td>
<td>38 (4.4)</td>
<td>0.61</td>
<td>18 (3.7)</td>
<td>26 (4.7)</td>
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<tr>
<td><strong>Stroke</strong></td>
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<td></td>
<td>38 (3.6)</td>
<td>7 (4.1)</td>
<td>31 (3.6)</td>
<td>0.73</td>
<td>24 (4.9)</td>
<td>14 (2.5)</td>
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<tr>
<td><strong>TIA</strong></td>
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<td></td>
<td>22 (2.1)</td>
<td>5 (2.9)</td>
<td>17 (1.9)</td>
<td>0.39</td>
<td>13 (2.6)</td>
<td>9 (1.6)</td>
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<tr>
<td><strong>Thromboembolism</strong></td>
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<td></td>
<td>8 (0.8)</td>
<td>2 (1.2)</td>
<td>6 (0.7)</td>
<td>0.62</td>
<td>5 (1.0)</td>
<td>3 (0.5)</td>
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<tr>
<td><strong>Vascular disease</strong></td>
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<td></td>
<td>111 (10.7)</td>
<td>11 (6.4)</td>
<td>100 (11.5)</td>
<td>0.05</td>
<td>75 (15.3)</td>
<td>36 (6.5)</td>
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<tr>
<td><strong>Smoking</strong></td>
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<tr>
<td>Ex-smokers</td>
<td>188 (18.4)</td>
<td>33 (19.9)</td>
<td>155 (18.1)</td>
<td>0.77</td>
<td>177 (36.8)</td>
<td>11 (2.0)</td>
</tr>
<tr>
<td>Current smokers</td>
<td>67 (6.5)</td>
<td>12 (7.2)</td>
<td>55 (6.4)</td>
<td>--</td>
<td>58 (12.1)</td>
<td>9 (1.7)</td>
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<tr>
<td>No smokers</td>
<td>768 (75.1)</td>
<td>121 (72.9)</td>
<td>647 (75.5)</td>
<td>--</td>
<td>246 (51.1)</td>
<td>522 (96.3)</td>
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<td><strong>ECG in the last 2 years</strong></td>
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<td></td>
<td>800 (76.7)</td>
<td>131 (76.6)</td>
<td>669 (76.7)</td>
<td>0.97</td>
<td>395 (80.4)</td>
<td>405 (73.4)</td>
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<tr>
<td><strong>Previous symptoms</strong></td>
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<tr>
<td></td>
<td>283 (27.2)</td>
<td>36 (21.1)</td>
<td>247 (28.4)</td>
<td>0.05</td>
<td>110 (22.4)</td>
<td>173 (31.4)</td>
</tr>
<tr>
<td><strong>Age, mean (y)</strong></td>
<td>73.1 (SD:7.8)</td>
<td>74.1 (SD:8.3)</td>
<td>72.9 (SD:7.7)</td>
<td>0.06</td>
<td>73.3 (SD:7.8)</td>
<td>73.0 (SD:7.8)</td>
</tr>
</tbody>
</table>

85% corresponded to persistent AF and a 15% to paroxysmal AF. (Table 2) shows the results of comparing demographic characteristics and the prevalence of the cardiovascular risk factors for the different subtypes of AF. Subjects with AF had significantly higher prevalence of most of the AF risk factors than the subjects without AF. The undiagnosed AF patients had not significantly differences in age (p 0.61), gender (p 0.54), hypertension prevalence (p 0.29) or DM2 (p 0.25), antecedents
of vascular diseases as ischemic cardiopathy, stroke or TIA and heart failure (p 0.10), CHA2DS2-VASc score (p 0.17). There were significant differences in a lower prevalence of treatment with OAC (12.7% versus 78.3%, p<0.001) and in the practice of an ECG in the last two years (82.6% versus 96.9 %, p=0.04).

The logistic regression analysis (Table 3) showed that the undiagnosed AF was associated with the profile of a 75-year-old man with previous medical history of heart failure, who lives in a rural area and has not had any ECG performed in the last two years. The interaction between “to be from rural areas (<1000 inhabitants)” and “to have an ECG performed in the last two years” was statistically significant (p=0.013). The variable “rural” carried a high risk of undiagnosed AF but when an ECG was performed, it had a high protective effect (OR 0.02 IC95% 0.00-0.44).

**Discussion**

It is generally acknowledged that AF incidence and prevalence are increasing due to growing numbers of older people but a wide range of uncertainty exists around the magnitude of future trends by differences in study design, covered time period, birth cohort, and temporal effects. There are as well as improvements in AF diagnosis due to increased use of diagnostic tools and health care awareness [20]. This report is one of many articles dealing with the AF in developed countries, but gives special emphasis incorporating the undiagnosed population, a segment of the patient population most often overlooked. It tries to quantify undiagnosed AF prevalence and has evaluated the factors associated with the undiagnosed AF. We found an overall AF prevalence of 10.9% and previously
undiagnosed AF of 2.2%. These data means that a 20.2% of the overall AF cases were undiagnosed. In addition, that overall AF prevalence increases with age especially in individuals over 70 years old. From the sixties to over eighties the prevalence increases by 10 times and the relationship between man and woman changes from 4:1 to 1:1. Eventually this percentage of undiagnosed AF should be added to percentage of known FA no treated with ACO which would mean about 40-50% [21] of overall AF. In the study’s territory, the percentage of people over 80 years old increased 68% in the period 1986-2006 which means the proportion of people over this age increases from the 3.5% to 6% [22] from which 60% are female. Clearly, it should have serious implications for the planning of health and welfare systems not only because of global burden of continuous increase [3,8,9] of AF prevalence, but because the undiagnosed group is not treated with OCA and should be included in many studies which found an underestimate of oral anticoagulants in atrial fibrillation [14,23-25] and by the increased benefit of the OCA elderly of the patients [26].

The lower share of the population with AF that is diagnosed the lower will be the share with anticoagulation treatment. Each patient with AF and thromboembolic risk factors who is not treated with anticoagulation will, in monetary terms, be in on an added financial burden on society [27-29], which is double that of the treated patient, because of their higher risk for brain vascular complications. Because a majority of patients with AF with increased risk for stroke had not received anticoagulation therapy, there is a large potential for improvement if the primary care professionals take a more proactive attitude of opportunistic case finding, regardless of the reason of the patient’s visit.

When additionally it was stratified by sex, overall AF had a higher prevalence in men in all age groups except in group over the eighties, where women achieved the highest prevalence. This fact has been also observed in few articles [13,15,30,31]. In a recent study, it has been found a slight decrease in the AF prevalence in people older than 85 years old for both, men and women [32] but in fact that article mentioned that woman never went beyond men AF prevalence.

It exists a wide range of uncertainty [20,32-34] around the AF studies design. It is well known that AF prevalence is considerably higher in hospitalized patients especially in internal medicine and geriatric wards (31% for patients ≥70-year-old) [35] than in primary care [36-38]. We included a proportional sample of the subjects who were attended at their homes or at nursing care or old people’s homes. Given the patients who did not visit the centre in the past 3 years, they have been excluded, presumably these relatively healthier individuals may be less likely to be diagnosed with AF and therefore the prevalence estimates that the paper may be exaggerated. However, the analysis of the primary care systems’ use excludes the 7.5% of the rest of the population with risk to suffer from AF.

The particular paroxysmal nature of most AF cases at its starting point [10] makes difficult to establish the true AF incidence. In addition, as we have observed in this study, an important part of these patients with cardiovascular co morbidities have not got an ECG in the last two years. It is for all these arguments that using just an ECG study is probably not sensible enough to diagnose a new AF. Because of that, other studies tried to combine at least a single ECG with medical records review [15,36,38,39] and some use other mixed strategies [40] in order to improve the probability of AF detection: patient’s medical history review; ECG recording [41] (24-48 hour Holter monitoring) but its high cost presents a major obstacle in large studies and may underestimate the true prevalence of AF, mainly the paroxysmal AF particularly if the burden is low [43]; cardiac invasive devices that detected a 42% of undiagnosed AF [43] and have substantially improved the detection of silent paroxysmal AF in patients with a recent ischemic stroke/TIA [44]. Nevertheless, until these new external devices can be broadly used, and probably in our socioeconomic context, the ECG study combined with medical history review will still be the best non-invasive feasible strategy to identify individuals with AF.

In this study we have used the term “Overall AF prevalence”, that have been used in epidemiologic studies by several authors [2,32,45] to refer the sum of previously undiagnosed and previously diagnosed AF prevalence. One of the most striking finding of this work has been the high overall AF prevalence that we observed. The fact that our study was performed in a primary care context and included a 10% of the studied people who were attended at their homes or at nursing care or old people’s homes, probably influenced in this high prevalence. Some studies [12,32] have speculated that these people could produce an increase of the AF prevalence. Previous studies [14,15,36] obtained a prevalence between 6.1-10.2% although included patients ≥18-year-old, or did not include patients visited at home or at care institutions, or excluded undiagnosed AF.

We also defined “Undiagnosed AF prevalence” as the percentage of people with an AF positive ECG performed at the moment of the study who did not have any previous medical record of an AF diagnosis independent of they had or not been previously studied. This term has also been previously used by few authors [12-15]. Other authors have used it as equivalent to prevalence of newly diagnosed AF [38] detected in some screening studies, or as the term undetected AF [42,46], and as unrecognized AF [47]. In our study represented a 2.2% of previously undiagnosed or the 20.2% of overall AF. In others[33,48] it was between 25-35%; or newly diagnosed AF (SAFE, England) [38] of 1.63%; or undiagnosed AF ≥85-year-old (England) [49] of 3.8%; (Norway) [12] of 1%; (Spain) [13-15] of 0.5-1.7%.

The logistic regression analysis performed in this study also demonstrated that age over 75 years old, men gender, previous chronic heart failure history, an absence of a previous ECG in the last two years and living in rural environment were the
major risk factor to have an undiagnosed AF. This supports the idea that this person could also be the result of an inadequate evaluation especially those with these clinical and demographic characteristics, and this reinforces the idea that AF screening must not be just a current opportunistic activity, but it should be an active practice to identify additional AF cases. It has been clearly demonstrated [36] that active screening for AF detects additional cases over current practice and that the most efficient method of screening is opportunistic pulse taking with follow-up electrocardiography specially in patients with multiple cardiovascular conditions [50]. On other hand, the evolution of the primary care attention in our country is lead to evaluation and distribution of the sanitary resources taking into account the concentration of the population. This fact together with the ageing of the population could provoke differences on accessibility, especially in those smaller central populations where precisely the older population live. This reason would be the explanation of the results of undiagnosed AF.

Since this is a study of subjects registered in the public primary care system, it is possible that a higher frequentation of AF patients or patients with AF risk in a context of high ageing population could produce an artificial increase of prevalence described. However, since an ECG performing is not a highly sensitive system to detect AF prevalence we should expect that a portion of them with AF could have not been detected.

Conclusions
The overall AF prevalence is 10.9% for >60-year-old people and it is strongly associated with ageing and male gender; from the sixties to the eighties increased by 10 times and changed the proportion man/woman from 4:1 to 1:1. The undiagnosed AF was 2.2% (CI95% 1.3-3.1). In this percentage untreated cases should expect that a portion of them with AF could have not been detected.

List of abbreviations
AF: Atrial fibrillation
AFABE: Atrial Fibrillation Audit in Baix Ebre
CHA₂DS₂-VASc: Congestive heart failure (or Left ventricular systolic dysfunction), Hypertension: blood pressure consistently above 140/90 mmHg (or treated hypertension on medication), Age ≥75 years, Diabetes Mellitus, Prior Stroke or TIA or thromboembolism, Vascular disease (e.g., peripheral artery disease, myocardial infarction, aortic plaque), Age 65–74 years old, Sex category (i.e., female gender)
CVRF: Cardiovascular risk factor
DM2: diabetes mellitus type 2
ECG: Electrocardiogram
GP: General practitioner
HAS-BLED: Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly
HF: Heart failure
OAC: Oral anticoagulation
PC: Primary care
SD: Standard Deviation
TIA: Transient Ischemic Attack.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions

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