Title: OPPORTUNISTIC SCREENING FOR ATRIAL FIBRILLATION VERSUS DETECTING SYMPTOMATIC PATIENTS AGED 65 YEARS AND OLDER: A CLUSTER-CONTROLLED CLINICAL TRIAL

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Abstract

-Objective: The goal of this study was to assess the effectiveness of opportunistic screening through pulse palpation in the early detection of atrial fibrillation in subjects aged ≥ 65 years versus detection through an active search for patients with symptoms and/or complications and sequelae associated.

-Material and methods: This was a cluster randomized controlled trial performed in 48 primary care centers of the Spanish National Healthcare System. A total of 368 physicians and nurses were randomized. The researchers in the Experimental Group (EG) performed opportunistic screening for auricular fibrillation, whereas the researchers in the Control Group (CG) actively searched for symptomatic patients. An ECG was performed on patients found to have an irregular heartbeat to confirm the diagnosis of auricular fibrillation.

-Results: A total of 5,465 patients with a mean age of 75.61 were recruited for the EG, and 1,525 patients with a mean age of 74.07 were recruited for the CG. Of these, 58.6% were female, without significant differences between groups. Pulse was irregular in 4.3% and 15.0% of the patients in the EG and the CG, respectively ($p<0.001$). A total of 165 new cases of atrial fibrillation were detected (2.3%), 1.1% in the EG and 6.7% in the CG (adjusted OR: 0.29; 95%CI: 0.18-0.45).

-Conclusions: Case finding for atrial fibrilation in patients aged ≥ 65 years with symptoms or signs suggestive of atrial fibrilation is a more effective strategy than opportunistic screening through pulse palpation in asymptomatic patients.

-Trial registration: the trial is registered in ClinicalTrials.gov (NCT01291953; February 8, 2011).

-keywords: atrial fibrillation; opportunistic screening; case finding; heart rhythm disorders.

Resumen

-Objetivo: El objetivo de este estudio fue evaluar la eficacia del cribado oportunista a través de la palpación del pulso para la detección de fibrilación auricular en sujetos asintomáticos de edad> 65 años frente a la búsqueda activa de pacientes ≥ 65 años con síntomas y/o complicaciones y secuelas asociadas.

-Material y métodos: Se realizó un ensayo clínico controlado aleatorizado por cluster en 48 centros de atención primaria del Sistema Nacional de Salud español. Se aleatorizó a un total de 368 médicos y enfermeras. Los investigadores del grupo experimental (GE) realizaron el cribado oportunista para la fibrilación auricular, mientras que los investigadores del grupo control (GC) buscaron activamente en pacientes sintomáticos. Se realizó un ECG en los pacientes que tenían un pulso irregular para confirmar el diagnóstico de fibrilación auricular.

-Resultados: Un total de 5.465 pacientes con una edad media de 75,61 fueron reclutados para la GE y 1.525 pacientes para el GC, con una edad media de 74,07. El 58,6% eran mujeres, sin diferencias significativas entre los grupos. El pulso era irregular en el 4,3% y el 15,0% de los pacientes del GE y el GC, respectivamente (p <0,001). Se detectaron un total de 165 nuevos casos de fibrilación auricular (2,3%), el 1.1% en el GE y el 6,7% en el GC (OR ajustada: 0,29; IC del 95%: 0,18-0,45).

-Conclusiones: la búsqueda activa a través de la palpación del pulso de fibrilación auricular en pacientes de edad ≥ 65 años con síntomas o signos sugestivos es una estrategia más eficaz que el cribado oportunista en pacientes asintomáticos.

-Registro del Ensayo clínico: registrado en ClinicalTrials.gov (NCT01291953; Febrero 2011).

-Palabras clave: fibrilación auricular; cribado oportunista; búsqueda de casos; trastornos del ritmo cardiaco

1. Introduction

Atrial fibrillation (AF) is the most frequent type of sustained arrhythmia and one of the arrhythmias with higher associated morbidity and mortality rates. In Spain, the global prevalence of AF is estimated to be 4.4%, which increases to 9.3% in patients aged between 70-80 years, and to 17.7% in patients over 80 years[1]. Similarly, the PREV-ICTUS study performed in patients older than 60 years reported a prevalence of 8.5%[2]. In Europe, the Rotterdam study[3] analyzed a cohort of patients older than 55 years and found a prevalence of 5.5%.

The clinical relevance of AF lies in the fact that, in its presence, the risk of having an ischemic stroke increases by 3.5% per year from 70 years of age. This risk can increase up to 20 times. Fifteen percent of ischemic strokes are attributed to this type of arrhythmia; strokes related to AF are more severe, associated with a higher degree of disability and greater healthcare costs[4].

A peculiarity of this arrhythmia is that it is frequently diagnosed by chance (subclinical AF). The FIATE registry revealed that AF was incidentally diagnosed in 26% of patients, of which 28% had unspecific symptoms (dizziness, fatigue, instability, anxiety or nervousness)[5]. The OFRECE study[1] revealed that 10% of patients with AF were unaware they were affected by the disease. The studies by Labrador MS et al[6] and Wheeldon NM et al[7] reported a prevalence of undiagnosed AF at 8.6% and 7.7%, respectively, in patients aged >65 years. Another study involving patients with a pacemaker revealed that 10.1% had subclinical atrial tachyarrhythmias, which was associated with a higher risk of having AF, an ischemic accident or systemic embolism[8]. The SMART study confirmed that one out of nine cryptogenic strokes had an underlying AF, whereas only 6% of strokes were symptomatic[9].

A test with high specificity should be developed to identify patients at risk of having subclinical or asymptomatic AF[10]. Although numerous methods have been used for the early detection of arrythmia[11], the most common is to take a patient's pulse –either systematically (population screening) or through the use of an opportunistic approach (when patients are seen for other health problems)–, and if the pulse is irregular, to perform an ECG[12-16]. This approach has been proven to have high sensitivity (94%) but low specificity (72%)[17].

To date, only two systematic reviews of studies that assess the early detection of AF have been published[18,19]. Amongst these studies opinions vary on best practices. Cochrane et al. concluded that the detection of AF increased both through opportunistic and systematic

screening, as compared to routine practice. However, their conclusions are based on the results of a single study. Some primary prevention guidelines recommend pulse palpation as an effective method for the early detection of AF in patients older than 65 or 75 years[20,21]. However, a recent publication by the UK NSC on screening for AF in adults does not recommend pulse palpation for the early detection of AF[22] and neither the US Preventive Services Task Force, and the Canadian Task Force on Preventive Health Care, said screening includes among its recommendations[23,24]. Thus, detection methods remain a controversial issue.

Primary Care providers are in a privileged position to be proactive with patients consulting for emerging or non-specific symptoms and thus make early detection of serious health problems.

Given the scarcity of evidence available, the main goal of this study was to assess the effectiveness of opportunistic screening through pulse palpation in the early detection of AF in subjects aged >65 years versus detection through an active search for patients with symptoms and/or complications and sequelae associated with AF.

2. Material and methods

2.1. Design

The study protocol has been described in detail elsewhere[25]. This was a multicenter, parallel-arm (Experimental Group –EG– versus Control Group –CG) cluster-controlled study. The healthcare professionals included were randomized to perform either opportunistic screening for AF or detection through identification of AF symptoms. The duration of the study was 24 months, and the field work took 18 months.

2.2. Participants

General practitioners and nurses from the Spanish National Health System were invited to participate in the study. Criteria for inclusion in the study consisted of being aged ≥ 65 years, attending the health center for other health problems and giving informed consent. Patients with a previous diagnosis of AF were excluded.

2.3. Sample size

The main endpoint was the proportion of new cases of AF detected. The sample size was calculated using the results reported by Fitzmaurice[14] by using the following criteria: Risk in exposed subjects: 1.63%; risk in non-exposed subjects: 1.012%; relative risk: 1.62; ratio: 2/1; 95% confidence interval, and an 80% precision. The sample size obtained was 7,722 subjects for the EG and 3,861 subjects for the CG. A non-response rate was estimated at 10% and adjustment was calculated according to the formula: Nf= Ni [1/(1-R)]=7,722 [1/(1-0.10)]= 8,580 (GE) and Nf of the CG= Ni [1/(1-R)]=3,861 [1/(1-0.10)]= 4,290 subjects in total. Estimates of intracluster correlation coefficient (ICC) in clinical trials in primary care cluster show that are generally less than 0.05 [26]. This translates CCI for a cluster size of 15, in a design effect corresponding to a factor of 1.7. Due to the cluster design nature of the study, it was necessary to recruit 12,870 patients from at least 100 healthcare professionals.

2.4. Randomisation

Randomization was centralized and stratified by type of healthcare professional (physician versus nurse) using the EPIDAT 3.1 software package. Consecutive sampling was performed by professionals for patient selection.

2.5. Study variables

The study variables are shown in table 1.

2.6. Intervention

The interventions involved:

-EG: screening for AF was performed on all patients seen by participating healthcare professionals, regardless of the reason for the visit.

-CG: screening was performed on any patient having symptoms suggestive of AF[27] (general discomfort, dyspnea, chest pain, palpitations, dizziness, decreased resistance to physical activity), complications or sequelae potentially attributable to AF (stroke and TIA).

Patients included in the study were informed of the goal of the study and were asked to sign an informed consent form. Next, their pulse was measured and if irregular, an ECG was performed to confirm the diagnosis.

The action program was as follows:

1. A Data Collection Form and a Procedure Manual including a Clinical Protocol for the Management of AF was designed[27].

2. A pilot study on a sample of 20 patients randomly selected by five physicians and five nurses from five primary care centers was conducted. The acceptability of the target population was high.

3. A communication campaign was launched using the directory of members of the Spanish Society of Family and Community Medicine and a directory of collaborators of the Family and Community Teaching Unit of Cordoba. Invitations were posted by e-mail to potential participants.

4. Next, participating healthcare professionals participated in a face-to-face training session where the procedures of the protocol were explained and they received training in pulse measuring procedures. At the end of the training session, inter-observer concordance in pulse measuring was evaluated. Each professional was asked to measure the radial pulse of the subject to their left and right and record it on a data collection sheet (regular versus irregular pulse). Reproducibility was found to be satisfactory (simple concordance rate=98.8%). Although the studies performed confirm the validity of pulse palpation (sensitivity=76.4%-90.0%; specificity=71.0%-96.9%)[17], to assess the reliability of the diagnosis of AF, the participating professionals were asked to interpret four ECGs selected by a cardiologist (two were suggestive of AF and two showed sinus rhythm) in an independent and blind manner. Simple concordances rates ranged between 83.7% for normal ECG and 91.4% for ECG showing AF.

5. A pulse was considered to be irregular when palpation showed an alteration or irregularity in rhythm for at least 15 seconds. When the pulse was found to be irregular, a 12-lead ECG was performed (along with a long L I-II-III strip. An ECG to confirm or rule out arrhythmia was also performed to patients with questionable or inconclusive pulse. Apart from AF, professionals were asked to check for other electrocardiographic alterations (table 1). ECGs were performed by participating family physicians and in doubtful cases by a cardiologist. In

186 patients with regular pulse ECG were asked to investigate other possible cardiac abnormalities, so in these patients the protocol was not strictly followed.

2.7. Statistical analysis

Statistical analysis was performed using the EPIDAT 3.1, SPSS 17.0 and MLwiN 2.02. software packages. A descriptive analysis was performed. To check the differences between the groups and previous verification of normality (Shapiro-Wilk), Chi-squared and T Student tests was applied. The relationship between the type of intervention and AF was assessed by the chi-squared test ($p<0.05$). We also calculated the Relative Risk (RR), Absolute Risk Reduction (ARR), and the Number Needed to Screen (NNS). Multivariate analysis was performed to adjust the main dependent variable (AF) for prognostic variables or predictors and/or confounders. Since randomization was by cluster, a multi-level regression analysis was first performed (level 1: professional; level 2: patients). The results showed that the potential cluster effect did not have any influence; therefore, we performed a multiple logistic regression analysis. Modeling was performed using the *Enter* method in the SPSS software package. The goodness of fit of the model was evaluated by the Hosmer-Lemeshow test.

2.8. Ethical aspects

The study was approved by the Ethics Committee for Clinical Research of Córdoba and the Ethics Committee for Clinical Research of Mataró Hospital, Barcelona. The study design was developed according to CONSORT Declaration recommendations for cluster-randomized clinical trials[25] . The trial was registered at Clinicaltrials.gob (NCT01291953).

3. Results

A total of 218 general practitioners and 101 nurses from 48 primary care centers located in 20 provinces in Spain performed patient recruitment. Figure 1 shows a diagram of the study. A total of 6,990 patients were recruited (5,465 for the EG and 1,525 for the CG).

Table 2 shows an analysis of the study variables concerning both healthcare professionals and patients by group. Patient's mean age was higher in the CG as compared to the EG (75.61 vs. 74.07). An appreciable difference was observed in the comparison of groups by age, as there were more patients in the 80-85 year and >85 years category in the CG (9.3 % vs. 5.6%). In total, 63.4% of patients were recruited by GPs versus 36.6% who were enrolled by nurses. A total of 90.2% of patients were recruited in primary care. A higher number of cardiovascular risk factors and associated morbidity (obesity, alcoholism, tobacco use, heart failure, hyperthyroidism and valvular heart disease) were observed in CG patients, as compared to EG patients.

Pulse palpation revealed an irregular pulse in 234 EG patients (4.3%), and the results were uncertain or inconclusive in 108 (2.0%). The proportion of patients in the CG with an irregular pulse was 15.0%, and pulse could not be certainly determined in 7.6%.

In respect to the reasons for the medical visit, 87.9% of EG patients had no AF symptoms versus 3.0% of CG patients who had no AF symptoms but had some complication or sequelae suggestive of AF (frequently, a cerebrovascular stroke). The most frequent symptoms were: dyspnea, dizziness, palpitations, chest pain and decreased resistance to physical activity.

A total of 164 new cases of AF (2.34%) were detected, of which 61 were EG patients (1.1%) and 103 were GC patients (6.8%). As shown in table 3, the RR was 0.16 (95%CI:0.11-0.21), the ARR was 5.70% (95%CI:4.77-6.49%) in favor of the CG, and the NNS was 17.7 (95%CI:14.4 to 23.0). Other electrocardiographic alterations were detected in 4.4% of patients (2.8% in the EG vs. 10.0% in the CG). In this case, the RR was 0.20 (95%CI:0.16-0.25), the ARR was 9.0% (95%CI:8.0-11.0%) and the NNS was 10.64 (95%CI:8.99-13.02).

The effects of the two interventions tested for the detection of new cases of AF are shown in table 4. Logistic regression was performed for adjustment for the independent variables. The OR for the variable "type of intervention" was 0.29 (95%CI:0.18-0.45).

4. Discussion

This study reveals that an active, selective search for symptomatic patients allows detection of up to 71% more new cases of AF (adjusted OR=0.29) than opportunistic screening through pulse palpation indiscriminately performed on all patients aged 65 years or older attended by a primary care center of the Spanish National Health System.

For a detection test to be recommended as an effective screening method, it must fulfill certain requirements concerning:

- The condition, such as prevalence, relevance, defined latency period, cost-effectiveness, etc;
- the method, which must be simple, safe, valid, reliable, efficient and acceptable by the target population;
- the confirmatory diagnosis and treatment, with evidence of effectiveness, possibility of performing it in the pre-symptomatic phase;
- and the preventive program, which must be evaluable, acceptable and feasible[7].

Screening for AF through pulse palpation complies with many of, though not all of, these requirements.

At present, only two approaches are used for the early detection of AF: systematic screening (an ECG is performed on all patients) or opportunistic screening (pulse is measured on all patients and, when irregular, an ECG is performed to confirm the diagnostic). To assess the effectiveness of these tests in detecting AF, they have to be compared with the effectiveness of routine practice[18]. In our study we tested an alternative approach: comparing opportunistic screening versus an active, selective search for patients (case finding) with symptoms and/or signs suggestive of AF.

Only two systematic reviews have been published that assess the early detection of AF[18,19]. Both concluded that the only evaluable study was one which compared two screening procedures (systematic versus opportunistic) with routine practice[14]. Several clinical guidelines recommend opportunistic screening for AF[20,21], although such recommendations are exclusively based on the results of the only study considered evaluable[14]. However, a number of recent reviews dismiss the feasibility of screening for AF[22]. This conclusion is primarily based on the fact that there is no solid

evidence demonstrating that screening patients with symptoms of AF is more effective than screening asymptomatic patients. To date, it has not been demonstrated that the prognosis of AF detected through screening is better than that when it is detected through routine practice.

Up to the present, no studies have been conducted that compare the effectiveness of actively searching for new cases of AF among patients with associated symptoms or complications versus screening through pulse palpation. A recent review highlights the relevance of subclinical AF in the prognosis and management of patients, since a timely preventive treatment would reduce the number of strokes and other associated complications[28].

In our study, the number of new cases of AF detected in the EG through pulse palpation (1.1%) was similar to that identified in previous studies (1.4% for patients aged ≥65 years) included in the systematic review by Lowres et al[19]; these studies used pulse palpation or ECG to perform a single time-point screening. It is also to be noted that the detection rate in the EG is similar to that reported in other studies such as that by Morgan et al[12] (1.3%) and SanMartin et al[29] (1.0%), and slightly lower when compared to Fitzmaurice et al[14] (1.6% through screening versus 1% detected through routine practice). Consequently, to detect new cases of AF using this method, between 71[30] and 167[14]more subjects would have to be screened. These modest results should be considered by the relevant authorities when it comes to implementing preventive activities, since such results may deter the authorities from supporting screening. On the other hand, if opportunistic screening is compared with an active search for symptomatic patients –as was done in our study–, only 17-18 patients older than 65 would need to be screened to detect an additional case of AF. These results clearly support active selective searching for symptomatic patients. In addition, we detected a high number of other ECG alterations, which were four times more frequent in the CG than in the EG. Some of these alterations –other atrial tachyarrhythmias– are related to the development of cryptogenic strokes.

This study has some limitations. The sample size was below the size initially calculated; therefore, a beta error may have occurred. To calculate the sample size, we based our investigation on the results of the study by Fitzmaurice[14], as it was the only study comparable with ours. However, given the noticeable difference found in the incidence of AF between the two groups, we believe that this study has enough statistical power to test the statistical hypothesis. Number of losses for not recruit patients was higher in the EG (15.0%) than in the CG (11.5%), particularly physicians (16/EG vs. 11/GC). This may influence the detection rate of AF cases in the

EG, since doctors performed more diagnostic research than nurses (OR=1.54); However, this variable (the provider) was controlled in the multivariate análisis. Additionally, some professionals who were willing to participate were excluded for not having recruited any patients; however, the number of exclusions was low and similar in both groups. There were no lost to follow-ups, which can be explained by the fact that no follow-up was required for these patients. Finally, researchers in the CG may have been more affected by the Hawthorne effect –or observer effect– than those in the EG. This may reduce the possibility of extrapolating the results obtained, since the effects obtained with respect to the procedures used in routine practice might be overestimated.

Although the results reported in this study may seem inconsistent with those of the systematic reviews published, this is not the case as, to date, opportunistic screening has never been compared with an active, selective search for patients with symptoms and/or signs suggestive of AF. In fact, this is the first study to compare and analyze differences between the two strategies. While further studies should be conducted to corroborate our findings, our conclusions are consistent with recent guidelines, which do not recommend performing non-selective opportunistic screening for AF in patients aged 65 years or older[22]. Moreover, organizations such as US Preventive Services Task Force and the Canadian Task Force on Preventive Health Care, not even take into account in its recommendations Opportunistic screening for atrial fibrillation[23,24]. Systematic population screening programme not recommended, clinical practice guidelines covered by NICE [31]. According to the recommendations on the management of AF made by NICE in 2014 [32], only it is advisable perform manual pulse palpation to assess for the presence of an irregular pulse that may indicate underlying atrial fibrillation in people presenting with any of the following symptoms or problems: breathlessness/dyspnoea, palpitations, syncope/dizziness, chest discomfort, or stroke/transient ischaemic attack.

In conclusion, screening for AF in patients aged ≥ 65 years with symptoms or signs suggestive of AF in primary care is a more effective strategy for the early detection of AF than opportunistic screening through pulse palpation in asymptomatic patients. Also, screening allows the diagnosis of other unnoticed heart rhythm disorders. The study results show that primary care professionals could detect up to 6% of new atrial fibrillation cases in people presenting any of the symptoms and signs, which can have significant positive impact on these patients care.

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Competing Interests

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References

1. Gómez-Doblas JJ, Muñiz J, Martin JJ, Rodríguez-Roca G, Lobos JM, Awamleh P, et al. Prevalencia de fibrilación auricular en Spain. Resultados del estudio OFRECE. Rev Esp Cardiol. 2014; 67: 259–69.

2. Cea-Calvo L, Redón J, Lozano JV, Fernández-Pérez C, Martí-Canales A, Llisterri JC et al. Prevalencia de fibrilación auricular en la población española de 60 o más años de edad. Estudio PREV-ICTUS. Rev Esp Cardiol. 2007; 60: 616–24.

3. Heeringa J, Van der Kuip DAM, Hofman A, Kors JA, Van Herpen G, Stricker B, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J. 2006; 27: 949–53.

4. Mérida-Rodrigo L, Poveda-Gómez F, Camafort-Babkowski M, Rivas-Ruiz F, Martín-Escalante MD, Quirós-López R, et al. Long-term survival of ischemic stroke. Rev Clin Esp. 2012; 212: 223–8.

5. Lobos-Bejarano JM, Castillo-Rodríguez JM, Mena-González A, Alemán-Sánchez JJ, Cabrera de León A, Barón-Esquivias G, et al. Características de los pacientes y abordaje terapéutico de la fibrilación auricular en atención primaria en Spain: Estudio FIATE. Med Clin (Barc). 2013; 141: 279-86.

6. Labrador García MS, Merino Segovia R, Jiménez Domínguez C, García Salvador Y, Segura Fragoso A, Hernández Lanchas C. Prevalencia de fibrilación auricular en pacientes > 65 años de un área de salud. Aten Primaria. 2001; 28: 648–51.

7. Wheeldon NM, Tayler DI, Anagnostou E, Cook D, Wales C, Oakley GDG. Screening for atrial fibrillation in primary care. Heart. 1998; 79: 50–5.

8. Healey JS, Connolly SJ, Gold MR, et al. Subclinical atrial fibrillation and the risk of stroke. N Engl J Med. 2012; 366: 120-9.

9. Flint AC, Banki NM, Ren X, et al. Detection of paroxysmal atrial fibrillation by 30-day event monitoring in cryptogenic ischemic stroke: The Stroke and Monitoring for PAF in Real Time (SMART) registry. Stroke. 2012; 43: 2788-90.

10. Documento marco sobre cribado poblacional. Ministerio de Sanidad y Consumo. Spain. Available from: http://www.msssi.gob.es/profesionales/saludPublica/prevPromocion/docs/Cribado_poblacional.pdf.

11. Quinn FR, Gladstone D. Screening for undiagnosed atrial fibrillation in the community. Curr Opin Cardiol 2014;29:28–35.

12. Morgan S, Mant D. Randomised trial of two approaches to screening for atrial fibrillation in UK general practice. Br J Gen Pract. 2002; 52: 373-4, 377-80.

13. Virtanen R, Kryssi V, Vasankari T, Salminen M, Kivelä SL, Airaksinen K Self-detection of atrial fibrillation in an aged population: the Lieto AF Study. Eur J Prev Cardio.l 2014; 21: 1437-42.

14. Fitzmaurice DA, Hobbs FDR, Jowett S et al. Screening versus routine practice in detection of atrial fibrillation in patients aged 65 or over: cluster randomised controlled trial. BMJ. 2007; 335: 383–8.

15. Sudlow M, Rodgers H., Kenny R. A, Thomson R. Identification of patients with atrial fibrillation in general practice: a study of screening methods. BMJ. 1998; 317: 327-8 .

16. Hobbs FD, Fitzmaurice DA, Mant J, Murray E, Jowett S, Bryan S, et al. Randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) vs. routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. Health Technol Assess. 2005; 9: 1-74.

17. Cooke G, Doust J, Sanders S. Is pulse palpation helpful in detecting atrial fibrillation? A systematic review. J Fam Pract. 2006; 55: 130–4.

18. Moran PS, Flattery MJ, Teljeur C, Ryan M, Smith SM. Effectiveness of systematic screening for the detection of atrial fibrillation (Review). Cochrane Database Syst Rev. 2013 Apr 30; 4:CD009586. Epub 2013 Apr 30.

19. Lowres N, Neubeck L, Redfern J, Freedman SB. Screening to identify unknown atrial fibrillation. A systematic review. Thromb Haemost [Internet]. Schattauer Publishers; 2013;110:213–22. Available from: http://dx.doi.org/10.1160/TH13-02-0165.

20. Camm J, Lip G, De Caterina R, Savelieva I, Atar D, Hohnloser SH, Hindricks G, Kirchhof P, ESC Committee for Practice Guidelines(CPG): 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. Eur Heart J. 2012; 33: 2719–47.

21. Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chatuverdi S et al. American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Functional Genomics and Translational Biology; Council on Hypertension. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014; 45: 3754-832.

22. The UK NSC recommendation on Atrial Fibrillation screening in adults. Available from: http://www.screening.nhs.uk/atrialfibrillation.

23. US Preventive Services Task Force. Recommendations for Primary Care Practice. Available from: http://www.uspreventiveservicestaskforce.org/Page/Name/recommendations.

24. Canadian Task Force on Preventive Health Care. Available from: http://canadiantaskforce.ca/.

25. Pérula de Torres LA, Martinez Adell MA, González Blanco V, Baena JM, Martín Rioboó E, Parras Rejano JM, et al. Opportunistic detection of atrial fibrillation in subjects aged 65 years or older in primare care: a randomised clinical trial of efficacy. DOFA-AP study protocol. BMC Family Practice. 2012;13:106. doi:10.1186/1471-2296-13-106.

26. Campbell MK GJ, Steen N, for the Changing Professional Practice in Europe Group. Sample size calculations for cluster randomised trials. J Health Serv Res Policy. 2000;5:12-6.

27. Camm J, Lip G, De Caterina R, Savelieva I, Atar D, Hohnloser SH, et al. ESC Committee for Practice Guidelines(CPG): 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. Eur Heart J. 2012; 33: 2719–47.

28. Hannon N, Sheehan O, Kelly L, Marnane M, Merwick A, Moore A et al. Stroke associated with atrial fibrillation-incidence and early outcomes in the North Dublin population stroke study. Cerebrovasc Dis. 2010; 29: 43-9.

29. Sanmartín M, Fraguela Fraga F, Martín-Santos A, Moix Blázquez P, García-Ruiz A, Vázquez-Caamaño M, et al. Una campaña de información y diagnóstico de la fibrilación auricular: la «Semana del Pulso». Rev Esp Cardiol. 2013; 66: 34–8.

30. Chen-Scarabelli C, Scarabelli TM, Ellenbogen KA, Halperin JL. Device-Detected Atrial Fibrillation What to Do With Asymptomatic Patients?. J Am Coll Cardiol. 2015; 65: 281–94.

31. The UK NSC recommendation on Atrial Fibrillation screening in adults. Available from: http://legacy.screening.nhs.uk/atrialfibrillation.

32. NICE Guidance CG 180. Atrial Fibrillation; the management of atrial fibrillation. June 2014. Available from: https://www.nice.org.uk/guidance/cg180/chapter/1-Recommendations#diagnosis-and-assessment.

Table 1. Study Variables

VARIABLES	DEFINITION
INDEPENDENT	
Study Group	EG: opportunistic detection CG: regular approach
Healthcare Professional involved	Physician vs. Nurse
Location	Province where the healthcare center is located
-Sociodemographic:	
Age	≥ 65 years
Sex	Male/female
Educational Level	No education, can read and write, primary education, secondary education, higher education
Civil Status	Single, married, widow/widower, divorced-separated
-Clinical and Functional Assessment:	
Place of enrollment	Office, emergency room, home visit
Symptoms and Signs	Asymptomatic, general discomfort, dyspnea, chest pain, palpitations, dizziness, decreased resistance to physical activity, embolic complications or exacerbation of heart failure.
Conditions (comorbidity) and associated health	Obesity, hypertension, diabetes mellitus, dyslipidemia, smoking, alcohol abuse, ischemic heart disease, peripheral artery disease, cerebrovascular accident (stroke, TIA), valvular heart disease, left ventricular hypertrophy, heart failure,

problems	hyperthyroidism, hypothyroidism, anxiety-depression, COPD, Other conditions
DEPENDENTS: **Peripheral arterial pulse** **Atrial Fibrillation** **Other ECG disorders**	Radial pulse: Regular, irregular or uncertain Atrial Fibrilation confirmed by electrocardiogram following clinical protocol Flutter, Extrasystole (ventricular / supraventricular / other), tachycardia, atrial Bigeminy, ventricular Bigeminy, bundle branch block, ventricular premature beats, bradycardia, Other.

Table 2. Sociodemographic and clinical characteristics according to the group

Healthcare Professional Variables	**Experimental Group** **n=158**	**Control Group** **n=161**
Sex: n (%)		
Men	46 (29.1)	50 (31.0)
Women	112 (70.9)	111 (69.0)
Occupation: n (%)		
Family Medicine	102 (64.6)	116 (72.0)
Nursing	56 (35.4)	45 (28.0)
Location: n (%)		
Barcelona	81 (51.3)	88 (54.7)
Córdoba	60 (38.0)	73 (45.3)
Other	17 (10.7)	0 (0.0)
Patient Variables	**Experimental Group** **n=5465**	**Control Group** **n=1525**
Age (years): Mean±SD (limits)	74.07±6.61 (65-103)	75.61±7.17 (65-104)
Age Groups (years): n (%)		
65 to 69	1874 (34.3)	422 (27.7)
70 to 74	1481 (27.1)	388 (25.4)
75 to 79	1153 (21.1)	334 (21.9)
80 to 84	653 (11.9)	239 (15.7)
85 or more	304 (5.6)	142 (9.3)
Sex: n (%)		
Men	2283 (41.8)	618 (40.5)
Women	3182 (58.2)	907 (59.5)
Civil Status: n (%)		
Married	3549 (64.9)	901 (50.1)
Widow/er	182 (3.3)	44 (2.9)
Divorced	288 (5.3)	92 (6.0)
Single	1446 (26.5)	488 (32.0)
Educational Level: n (%)		
No education	577 (10.6)	240 (15.7)
Can read and write	1934 (35.4)	573 (37.6)
Primary Education	1890 (34.6)	482 (31.6)
Secondary Education	691 (12.6)	156 (10.2)
Higher Education	373 (6.8)	74 (4.9)
Place of residence; n (%)		
Barcelona	3207 (58.7)	738 (48.4)
Córdoba	2187 (40.0)	787 (51.6)
Other	71 (1.3)	0 (0.0)

Table 2 (continuation)		
Patients recruited by occupation: n (%)		
Family Medicine	3402 (62.3)	1030 (67.5)
Nursing	2063 (37.7)	495 (32.5)
Place of patient recruitment: n (%)		
Office	5094 (93.2)	1217 (79.8)
Emergency Room	244 (4.5)	264 (17.3)
Home Visit	127 (2.3)	44 (2.9)
Arterial pulse: mean±SD (limits)	75.04±11.23 (41-180)	78.06±16.22 (40-180)
Signs and symptoms associated with potential AF: n (%)		
Asymptomatic	4803 (87.9)	45 (3.0)
Dyspnoea	224 (3.6)	432 (30.3)
Chest Pain	80 (1.4)	150 (10.2)
Palpitations	47 (0.8)	172 (12.2)
Dizziness	141 (2.5)	456 (27.2)
Decreased resistance to physical activity	59 (1.2)	107 (7.0)
Ankle edema	40 (0.7)	33 (2.4)
General Discomfort	26 (0.4)	88 (5.7)
Other	37 (0.7)	41 (2.7)
Number of signs and symptoms: mean±SD (limits)	0.17±0.52 (0-5)	1.40±0.76 (0-5)
Pulse rate: n (%)		
Regular	5123 (93.7)	1181 (77.4)
Irregular	342 (6.3)	342 (22.6)
Electrocardiogram results: n (%)		
-Performed (n=864;12,9%)	402 (7.8)	462 (32.3)
Normal	185 (3.4)	226 (14.8)
Atrial Fibrilation	61 (1.1)	104 (6.8)
Flutter	2 (0.1)	5 (0.3)
Ventricular premature beats	37 (0.7)	36 (3.0)
Supraventricular premature beats	53 (1.0)	42 (2.8)

Paroxysmal supraventricular tachycardia	3 (0.1)	4 (0.3)
Sinus tachycardia	2 (0.1)	11 (0.8)
Atrial tachycardia	0 (0.0)	1 (0.1)
Headphone bigeminy	2 (0.1)	5 (0.3)
Ventricular bigeminy	2 (0.1)	1 (0.1)
Branch block	7 (0.3)	23 (1.5)
Other changes on elechtrocardiogram	44 (1.0)	32 (2.3)
Artifact ECG	2 (0.1)	2 (0.2)
Morbidity: n (%)		
Obesity	871 (15.9)	294 (19.3)
Arterial hypertension	3543 (64.8)	1054 (69.1)
Mellitus diabetes	1530 (28.0)	437 (28.7)
Dyslipidemia	2431 (44.5)	635 (41.6)
Smoking	191 (3.5)	66 (4.3)
Acoholism	55 (1.0)	27 (1.8)
Ischemic heart disease	396 (7.2)	150 (9.8)
PAD	87 (1.6)	33 (2.2)
Cerebrovascular accident (Stroke, TIA)	218 (4.0)	69 (4.5)
Valvular	102 (1.9)	41 (2.7)
Left ventricular hypertrophy	57 (1.0)	17 (1.1)
Heart failure	80 (1.5)	35 (2.3)
Hyperthyroidism	28 (0.5)	18 (1.2)
Hypothyroidism	253 (4.6)	67 (4.4)
Anxiety-depression	294 (5.4)	72 (4.7)
COPD	300 (5.5)	91 (6.0)
Other conditions	2000 (36.6)	611 (40.0)
Number of conditions: mean±SD (limits)	2.32±1.48 (0-9)	2.48±1.41 (0-7)
Signs and symptoms associated with potential AF: n (%)		
Asymptomatic	4803 (87.9)	45 (3.0)
Dyspnoea	224 (3.6)	432 (30.3)
Chest Pain	80 (1.4)	150 (10.2)
Palpitations	47 (0.8)	172 (12.2)
Dizziness	141 (2.5)	456 (27.2)

Decreased resistance to physical activity	59 (1.2)	107 (7.0)
Ankle edema	40 (0.7)	33 (2.4)
General Discomfort	26 (0.4)	88 (5.7)
Other	37 (0.7)	41 (2.7)

ED: Standar deviation; ECG: electrocardiogram; COPD: Chronic obstructive pulmonary disease

Table 3. Cases of atrial fibrillation and other electrocardiographic alterations detected by group. Estimators of the intervention magnitude and impact

Group	Patients n (%)	FA cases n (%)	RR (95%CI)	ARR (95%CI)	NNS (95%CI)
Control	1525 (21.8)	103 (6.80)	0.16 (0.11-0.21)	5.70% (4.77-6.49%)	17.7 (14.4 a 23.0)
Experimental	5465 (78.2)	61 (1.10)			
Total	6990 (100.0)	164 (2.34)			
Group	Patients n (%)	Other electrocardiographic alterations n (%)	RR (95%CI)	ARR (95%CI)	NNT (95%CI)
Control	1525 (21.8)	155 (10.0)	0.20 (0.16-0.25)	9.0% (8.0-11.0%)	10.6 (9.0-13.0)
Experimental	5465 (78.2)	152 (2.8)			
Total	6990 (100.0)	307 (4.4)			

RR: Relative Risk; ARR: Absolute Risk Reduction; NNS: Number Needed to Screen; 95%CI: 95% Confidence Interval

Table 4. Detected cases of atrial fibrillation by group, adjusted according to the predictor variables studied

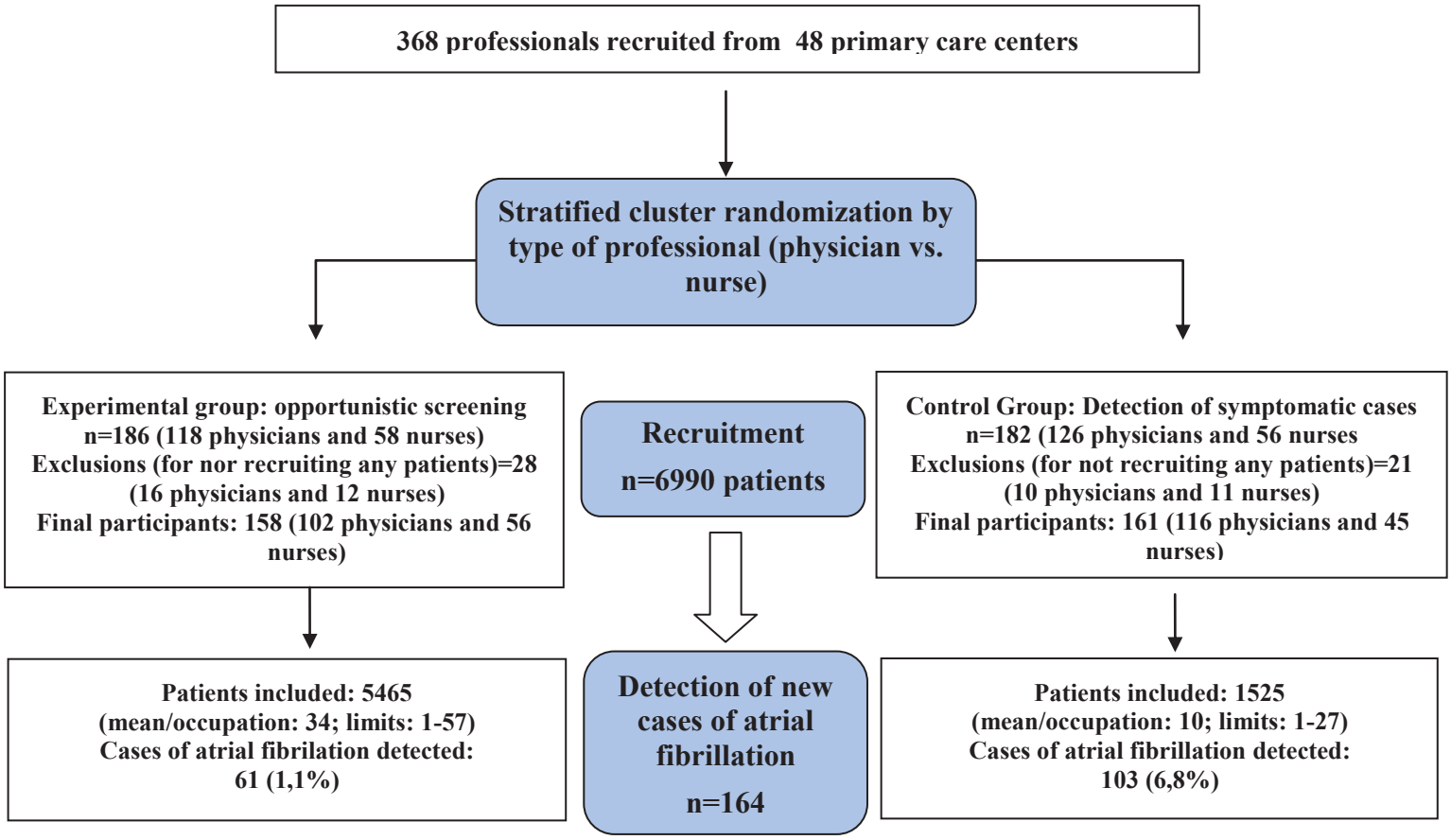
Variables in the model	B	p	OR	IC 95% de OR
Group (Experimental vs. Control)	-1.247	<0.001	0.29	0.18-0.45
Occupation (Physician vs. Nurse)	0.435	0.042	1.54	1.02-2.35
Place of recruitment (category of reference: office):				
Emergency Room	0.646	0.009	1.91	1.17-3.09
Home Visit	1.630	<0.001	5.10	2.68-9.72
Age group (category of reference: 65 to 69 years):				
70 to 74	0.388	0.194	1.47	0.82-2.65
75 to 79	0.594	0.048	1.81	1.00-3.27
80 to 84	1.122	<0.001	3.07	1.66-5.65
85 or more	1.670	<0.001	5.31	2.75-10.27
Sex (Men vs. Women)	0.722	<0.001	2.06	1.37-3.08
Civil Status (category of reference: widow/er)				
Married	0.062	0.780	1.06	0.69-1.65
Separated	-0.514	0.485	0.59	0.14-2.53
Single	0.296	0.455	1.34	0.62-2.92
Educational level (category of reference: no education):				
Can read and write	-0.285	0.214	0.75	0.48-1.19
Primary Education	-0.174	0.613	0.84	0.43-1.65
Secondary Education	-0.152	0.606	0.85	0.48-1.53

Higher Education	0.098	0.822	1.10	0.47-2.57
Number of symptoms	0.093	0.459	1.10	0.86-1.40
Arterial rate	0.075	<0.001	1.08	1.07-1.09
Obesity	0.600	0.062	1.82	0.97-3.42
High Blood Pressure	0.707	0.022	2.03	1.11-3.71
Diabetes Mellitus	-0.166	0.578	0.85	0.47-1.52
Dyslipemia	0.141	0.614	1.15	0.66-1.99
Tobacco use	0.592	0.237	1.81	0.68-4.81
Alcoholism	-0.192	0.799	0.83	0.19-3.62
Ischemic Heart Disease	0.257	0.526	1.29	0.58-2.86
Peripheral Artery Disease	1.340	0.009	3.82	1.40-10.44
Vasculocerebral Accident	0.189	0.698	1.21	0.46-3.14
Valvular heart disease	-0.820	0.344	0.44	0.08-2.41
Left Ventricular Hypertrophy	1.345	0.041	3.84	1.06-13.93
Heart Failure	0.175	0.808	1.19	0.29-4.92
Hyperthyroidism	0.211	0.840	1.23	0.16-9.56
Anxiety/Depression	0.030	0.965	1.03	0.26-4.03
Hypothyroidism	0.502	0.414	1.65	0.49-5.52
Chronic obstructive pulmonary disease	0.006	0.990	1.01	0.38-2.68
Number of pathologies	-0.320	0.135	0.73	0.48-1.10
Constant	-10.707			

n=6990; OR: Odds Ratio; 95%CI: 95% Confidence Interval; Omnibus test:515,886; p<0,001; Hosmer-Lemeshow test:4.606; p=0.799

Figure 1

Figure 1. Flowchart of the participants acording to the CONSORT Declaration



CONSORT

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Annex

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