Family Practice, 2014, Vol. 31, No. 3, 298–302
doi:10.1093/fampra/cmu011
Advance Access publication 12 April 2014

Is screening for AF worthwhile? Stroke risk in a screened population from the SAFE study

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Received November 15 2013; revised March 5 2014; Accepted March 10 2014.

Abstract

Introduction. Atrial fibrillation (AF) is an important independent risk factor for stroke and oral anticoagulation therapy provides a highly effective treatment to reduce this risk. Active screening strategies improve detection of AF in comparison with routine care; however, whether screen-detected patients have stroke risk profiles favouring anticoagulation is unclear. Using data derived from the screening for AF in the elderly (SAFE) study, the aim of this article was to determine if patients with AF detected *via* active screening have stroke risk profiles that warrant prophylactic anticoagulation.

Methods. Secondary analysis of data derived from 25 general practices within which cohorts of 200 patients were randomly allocated to opportunistic [pulse and electrocardiogram (ECG)] or systematic screening (postal invitation for ECG). Stroke risk assessment was undertaken using baseline data extracted from medical records and CHADS2 criteria. CHADS2 scores were compared between the screening groups.

Results. One hundred and forty-nine new cases of AF were detected, 75 *via* opportunistic screening and 74 *via* systematic screening. CHADS2 scores were ≥1 in 83% [95% confidence interval (CI) 72.6–89.6] of patients detected *via* opportunistic screening and 78% (95% CI 67.7–86.2) detected *via* systematic screening. There were no significant differences in stroke risk profiles of patients detected *via* opportunistic and systematic screenings.

Conclusion. Stroke risk profiles of patients detected *via* opportunistic and systematic screenings were similar. Data derived from the SAFE study suggest that active screening for AF in patients aged ≥65 years in primary care is a useful screening programme with 78–83% of patients identified eligible for anticoagulation treatment according to the CHADS2 criteria.

Key words: Anticoagulation, atrial fibrillation, primary care, risk factors, screening, stroke.

Introduction

Atrial fibrillation (AF) is an important independent risk factor for thromboembolic disease, particularly stroke with which it is associated with a 5-fold increase in risk (1). Prevalence data for AF have produced estimates of between 5% and 10% in the population aged >65 years. Randomized controlled trials have consistently shown that oral anticoagulation is highly effective for stroke prevention and meta analysis of these trials has shown a 68% relative risk reduction in patients with AF receiving oral anticoagulation therapy (2,3).

While oral anticoagulation therapy with warfarin is highly effective for stroke prevention in patients with AF, it is also associated with serious bleeding risk. For this reason, prior to

initiation of prophylactic anticoagulation in a patient with AF, it is necessary to determine if the risk of stroke is sufficiently high to outweigh the risk of serious bleeding. To determine whether a patient with AF is likely to benefit from anticoagulation therapy, the National Institute Health and Care Excellence recommends individual stroke risk assessment and stratification using the CHADS2 scoring criteria (4,5). CHADS2 is an acronym for the following clinical risk factors and their associated values; congestive heart failure, +1; hypertension, +1; aged ≥75 years, +1; diabetes mellitus, +1 and history of stroke or transient ischaemic attack (TIA), +2. Values are summed to give a total score and scores can be stratified into low, moderate and high stroke risk categories. A CHADS2 score ≥2 is a strong indication for anticoagulation (6). Prophylactic anticoagulation in patients with lower CHADS2 scores is less certain; however, the European Society of Cardiology and other guideline groups recommend anticoagulation in those with a CHADS2 score ≥1 (7,8).

Current evidence indicates that in the UK, AF is under-diagnosed and anticoagulation is under-prescribed with around half of patients with AF and stroke risk profiles favouring anticoagulation not receiving appropriate treatment (5,9). There is consensus among clinicians on the need for a national screening programme to increase the detection of AF; however, there remain reservations among policymakers as patients detected *via* screening may not be at high risk of stroke (10). Furthermore, there is uncertainty as to whether screen-detected AF carries the same risk of stroke as AF that is detected through routine clinical practice. While there is evidence to suggest that people with asymptomatic AF have similar risks of death and other major events to people with symptomatic AF, the 95% confidence intervals (CIs) around these estimates include the possibility that asymptomatic AF carries only two-thirds of the risk of symptomatic AF (11,12).

The screening for AF in the elderly (SAFE) study demonstrated that active screening for AF is more effective than routine care with opportunistic and systematic screening strategies yielding equivalent results (13,14). This study utilized data derived from the SAFE screening study to examine the potential impact of opportunistic and systematic screening strategies for AF with respect to identification of patients with a stroke risk profile favouring anticoagulation treatment. The aim of this article was to determine if patients with AF detected *via* active screening have stroke risk profiles that warrant anticoagulation.

Methods

Data were collected during SAFE study (13,14). This large-scale multi-centred, cluster-randomized controlled trial involved 50 UK primary care centres, randomized to either screening (intervention) or no screening (control). This article reports results of secondary analysis of data derived from the SAFE screening practices only, as data enabling the calculation of stroke risk scores were not collected within the practices randomized to the control arm of the study.

Full details of the SAFE study methodology have been previously reported (10). Within the practices randomized to screening, computerized searches were undertaken to identify all eligible patients aged ≥65 years. The practice disease register for AF was reviewed and computerized medical records of all eligible patients were searched using Read codes to extract data related to a diagnosis of AF. Once the searches for AF had been completed, cohorts comprising 200 patients were randomly selected from the list of eligible patients ≥aged 65. After sampling, within each practice 200 patients were randomized to opportunistic screening and 200 patients were randomized to systematic screening. At baseline, the medical records of all randomized patients were searched using Read codes to extract data related to a diagnosis of hypertension, congestive heart failure, diabetes mellitus, stroke and TIA. Practice disease registers were also reviewed to ensure that all data related to the presence of these stroke risk factors were captured.

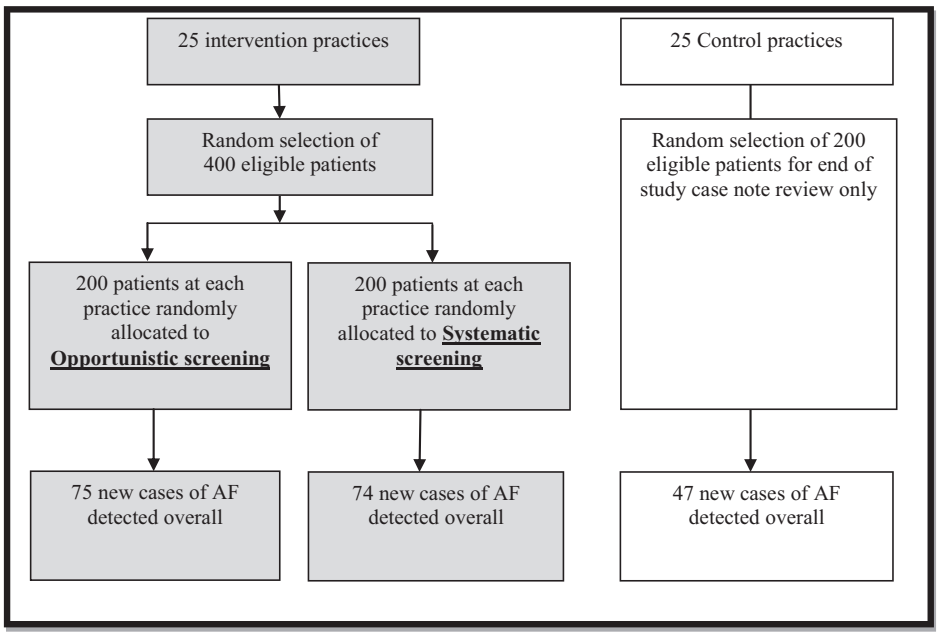
Patients allocated to the opportunistic screening arm had flags placed in their notes (electronic or paper), to prompt the practice nurse or GP to take the patients' pulse when they next attended the practice. If the pulse was found to be irregular, the patient was referred for a 12-lead electrocardiogram (ECG). All patients allocated to systematic screening were invited by post to attend a screening clinic for a 12-lead ECG.

Screening took place over a 12-month period in each practice between October 2001 and February 2003. At the end of the screening period, computer searches were re-run to identify all patients with a new diagnosis of AF. Overall, 149 new cases of AF were identified during the SAFE study. Seventy-five new cases of AF were detected within the opportunistic screening arm and 74 cases in the systematic screening arm (Fig. 1).

Using data collected from the computer searches conducted at baseline, CHADS2 stroke risk scores were calculated for all patients with AF detected *via* screening. The Chi-square test for independence with one degree of freedom was used to compare the prevalence of stroke risk factors in patients identified *via* opportunistic and systematic screenings and to compare the proportion of CHADS2 stroke risk scores ≥1 and ≥2 between the two screening groups. The Mann–Whitney *U*-test was employed to compare the distribution of CHADS2 stroke risk scores between the two screening groups.

Results

The baseline prevalence of CHADS2 criteria is reported in Table 1. The prevalence of CHADS2 criteria at baseline was similar for patients with AF detected *via* the two screening strategies. Of the 75 patients with AF detected *via* opportunistic



Only data derived from the intervention practices is presented in this paper. Data enabling calculation of CHADS2 score were not collected within the control practices.

Figure 1. SAFE study flow diagram showing new cases of AF detected in each arm of the study.

Table 1. Prevalence of clinical risk factors for stroke

	Opportunistic screening % (n = 75)	Systematic screening % (n = 74)	Opportunistic versus systematic P value
Cardiac failure	12.0 (9)	10.8 (8)	0.82 (X^2 = 0.05)
Hypertension	34.7 (26)	40.5 (30)	0.46 (X^2 = 0.55)
Age 75+	62.7 (47)	63.5 (47)	0.92 (X^2 = 0.01)
Diabetes	8.0 (6)	10.8 (8)	0.56 (X^2 = 0.35)
Stroke or TIA	5.0 (4)	9.5 (7)	0.34 (X^2 = 0.93)

Multiple risk factors were recorded per patient.

screening, 47 (62.7%) were aged ≥75 years, 26 (34.7%) had hypertension, 9 (12%) had cardiac failure, 6 (8%) had diabetes and 4 (5%) had a history of stroke or TIA. Forty-seven of the 74 (63.5%) patients with AF detected *via* systematic screening were aged ≥75 years, 30 (40.5%) had hypertension, 8 (10.8%) had cardiac failure, 8 (10.8%) had diabetes and 7 (9.5%) had a history of stroke or TIA.

CHADS2 stroke risk scores are reported in Table 2 and ranged from 0–4 for patients with AF detected *via* opportunistic screening and 0–5 in patients detected *via* systematic screening. The frequency of CHADS2 scores ≥1 in patients with AF detected *via* the two screening strategies was similar. Of the 75 patients with AF detected *via* opportunistic screening, 62 (82.7%, 95% CI 72.6–89.6) had CHADS2 scores ≥1. Fifty-eight of the 74 patients (78.4%, 95% CI 67.7–86.2) with AF detected *via* systematic screening had CHADS2 scores ≥1. The frequency of CHADS2 scores ≥2 in patients with AF detected *via* the two screening strategies was also similar with 22 (29.3%; 95 CI; 20.2–40.4) detected *via* opportunistic screening and 32 (43.2% 95% CI; 32.6–54.6) detected *via* systematic screening (P = 0.077). A Mann–Whitney U-test revealed no significant differences in the distribution of CHADS2 stroke risk scores between patients with AF detected *via* opportunistic screening (median = 1, n = 75) and systematic screening (median = 1, n = 74), U = 2560.5, Z = –0.86, P = 0.39.

Discussion

Using data derived from the SAFE study, this article aimed to determine if patients with AF detected *via* active screening have CHADS2 stroke risk scores that warrant anticoagulation. The data also allowed comparison of CHADS2 scores between

Table 2. Stroke risk scores for all new cases of AF detected within the two arms of the study

CHADS2 score	Method of detection		Stroke risk score ≥1 opportunistic versus systematic screening *P* value	Stroke risk score ≥2 opportunistic versus systematic screening *P* value
	Opportunistic screening % (*n* = 75)	Systematic screening % (*n* = 74)		
1	53.3 (40)	35.1 (26)	82.7% (95% CI; 72.6–89.6) versus 78.4% (95% CI; 67.7–86.2); $X^2 = 0.44$; $P = 0.51$	29.3% (95% CI; 20.2–40.4) versus 43.2% (95% CI; 32.6–54.6); $X^2 = 3.12$; $P = 0.077$
2	17.3 (13)	29.7 (22)		
3	8.0 (6)	5.4 (4)		
4	4.0 (3)	6.8 (5)		
5	0	1.4 (1)		

Mann–Whitney $U = 2560.5$, $Z = -0.86$, $P = 0.39$.

patients with AF detected *via* opportunistic and systematic screening, to determine whether patients detected *via* these screening strategies have different risk profiles and which strategy identifies patients most likely to benefit from oral anticoagulation therapy.

The data reported here indicate that patients with AF identified *via* opportunistic and systematic screening have a similar prevalence of stroke risk factors and similar stroke risk profiles. Furthermore, data suggest that 83% (95% CI 72.6–89.6) of patients with AF detected *via* opportunistic screening and 78% (95% CI 67.7–86.2) of patients with AF detected *via* systematic screening have stroke risk profiles favouring prophylactic anticoagulation. On this basis, it is likely that between 78% and 83% of patients aged ≥65 years with AF detected *via* active screening and subsequently treated in the primary care setting will derive some benefit from prophylactic anticoagulation. In addition, data suggest that potential benefits will be similar in patients with AF detected *via* opportunistic or systematic screening.

To be an effective intervention, an AF screening programme must improve detection of AF and provide benefit for patients with AF detected as result of screening (15). The SAFE study addressed a number of questions on the optimal screening strategy for AF in terms of what population to include and whether screening should be systematic or opportunistic. The principal conclusions from the SAFE study were that active screening will identify an additional third of cases of AF and opportunistic screening is as effective as systematic screening (13,14). In addition, economic analysis suggested that opportunistic screening costs less than systematic screening and is cost-effective in terms of cost per quality adjusted life year gained by reduced stroke incidence (16). Subgroup analysis exploring the potential impact of screening in patients at higher risk of stroke and based upon additional independent risk factors, such as previous diagnosis of heart failure, hypertension, stroke and TIA, also supported opportunistic screening over systematic screening in this population. The findings of the SAFE study clearly indicate that active screening (either opportunistic or systematic) increases the rate of detection of AF in an elderly community dwelling population compared with routine care. Whether early detection of AF through screening translates to improved clinical outcomes within the screened population, however, has yet to be fully elucidated (17).

The findings presented here should be interpreted with caution, since they are derived from secondary analysis of data from the SAFE study and the current analysis is underpowered to detect statistically significant differences in stroke risk scores between the two screening strategies. Another limitation is that CHADS2 data were not available for the SAFE study practices randomized to the control arm of the study. Comparison of stroke risk profiles of AF patients identified within the practices randomized to control (no screening) and within the practices randomized to intervention (active screening; either systematic or opportunistic) was not possible. It may be reasonable, however, to assume that patients detected *via* opportunistic screening consulting their GP in relation to symptoms and/or co-morbidity have a similar stroke risk profile to that of patients with AF diagnosed incidentally through routine care. No data to support this assumption is, however, currently available. An additional limitation of this study is that data enabling calculation of CHADS2 scores were derived from information routinely collected and recorded in computerized medical records. Randomization, however, should have ensured equal distribution of these limitations across the opportunistic and systematic screening arms.

Nevertheless, data presented in this article provide a useful insight into to the potential therapeutic consequences of active screening for AF in the >65s and indicate that 78–83% of patients with AF identified through screening would potentially benefit from prophylactic anticoagulation using a CHADS2 criteria of ≥1. Using the newer CHA2DS2-VASc score, it is likely that more patients would be eligible for anticoagulation, making a screening programme more cost-effective (18). Further research to investigate the effectiveness of anticoagulation in screen-detected patients versus non-screen detected patient is, however, required.

Declaration

Trial registration: current controlled trials ISRCTN19633732.
Contributions: the study was designed by DAF, FDRH and ETM and funding was secured by DAF and FDRH. ETM, JB and SJ undertook management of the study. JB undertook data collection and SJ and HS were responsible for data management and quality assurance. JB, RH and DM undertook all analyses for this sub-study. All authors contributed to data interpretation. JB and DM wrote the first draft of this paper and all authors were responsible for subsequent critical revision of the manuscript. DM is the corresponding author for this paper.

Funding: the Screening for Atrial Fibrillation in the Elderly study was funded by the National Health Service Research and Development Health Technology Assessment programme (96/22/11).
Ethical approval: favourable ethical opinion for the SAFE study was obtained from the West Midlands Multicentre research ethics committee.
Conflict of interest: none.

References

1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991; **22**: 983–8.
2. Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. *Arch Intern Med* 1994; **154**:1449–1457.
3. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med* 2007; **146**: 857–67.
4. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA* 2001; **285**: 2864–70.
5. NICE. Atrial Fibrillation (CG36). http://guidance.nice.org.uk/CG36 (accessed on 29 October 2013).
6. Camm AJ, Lip GY, De Caterina R *et al.*; ESC Committee for Practice Guidelines-CPG; Document Reviewers. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation–developed with the special contribution of the European Heart Rhythm Association. *Europace* 2012; **14**: 1385–413.
7. Skanes AC, Healey JS, Cairns JA *et al.*; Canadian Cardiovascular Society Atrial Fibrillation Guidelines Committee. Focused 2012 update of the Canadian Cardiovascular Society atrial fibrillation guidelines: recommendations for stroke prevention and rate/rhythm control. *Can J Cardiol* 2012; **28**: 125–36.
8. Gorin L, Fauchier L, Nonin E *et al.* Antithrombotic treatment and the risk of death and stroke in patients with atrial fibrillation and a CHADS2 score=1. *Thromb Haemost* 2010; **103**: 833–40.
9. Olesen JB, Torp-Pedersen C, Hansen ML, Lip GY. The value of the CHA2DS2-VASc score for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0-1: a nationwide cohort study. *Thromb Haemost* 2012; **107**: 1172–9.
10. Stott DJ, Dewar RI, Garratt CJ *et al.*; Royal College of Physicians of Edinburgh. RCPE UK Consensus Conference on 'Approaching the comprehensive management of atrial fibrillation: evolution or revolution?'. *J R Coll Physicians Edinb* 2012; **42** (suppl 18): 3–4.
11. Flaker GC. Is quality of anticoagulation a 'wild card' in the treatment of patients with atrial fibrillation? *Nat Clin Pract Cardiovasc Med* 2007; **4**: 72–3.
12. UK National screening committee. The UK NSC Policy on Atrial Fibrillation Screening in Adults. http://www.screening.nhs.uk/atrialfibrillation (accessed on 29 October 2013).
13. Fitzmaurice DA, Hobbs FD, 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.
14. Swancutt D, Hobbs R, Fitzmaurice D *et al.* A randomised controlled trial and cost effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in the over 65s: (SAFE) [ISRCTN19633732]. *BMC Cardiovasc Disord* 2004; **4**: 12.
15. UK National screening committee. Criteria for Appraising the Viability, Effectiveness and Appropriateness of a Screening Programme. http://www screening nhs uk/criteria/ (accessed on 29 October 2013).
16. Hobbs FD, Fitzmaurice DA, Mant J *et al.* A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. *Health Technol Assess* 2005; **9**: iii–iv, ix–x, 1–74.
17. Moran PS, Flattery MJ, Teljeur C, Ryan M, Smith SM. Effectiveness of systematic screening for the detection of atrial fibrillation. *Cochrane Database Syst Rev* 2013; **4**: CD009586.
18. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010; **137**: 263–72.