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

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Abstract

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

<table>
<thead>
<tr>
<th>CHADS2 score</th>
<th>Method of detection</th>
<th>Stroke risk score ≥1 opportunistic versus systematic screening</th>
<th>Stroke risk score ≥2 opportunistic versus systematic screening</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Opportunistic screening % (n = 75)</td>
<td>Systematic screening % (n = 74)</td>
<td>( P ) value</td>
</tr>
<tr>
<td>1</td>
<td>53.3 (40)</td>
<td>35.1 (26)</td>
<td>82.7% (95% CI; 72.6–89.6) versus 78.4% (95% CI; 67.7–86.2); ( \chi^2 = 0.44; P = 0.51 )</td>
</tr>
<tr>
<td>2</td>
<td>17.3 (13)</td>
<td>29.7 (22)</td>
<td>( \chi^2 = 0.51 )</td>
</tr>
<tr>
<td>3</td>
<td>8.0 (6)</td>
<td>5.4 (4)</td>
<td>( \chi^2 = 3.12; P = 0.077 )</td>
</tr>
<tr>
<td>4</td>
<td>4.0 (3)</td>
<td>6.8 (5)</td>
<td>( \chi^2 = 3.12; P = 0.077 )</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>1.4 (1)</td>
<td>( \chi^2 = 3.12; P = 0.077 )</td>
</tr>
</tbody>
</table>

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 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.

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References