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Research into practice:

management of atrial fibrillation in general practice

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BACKGROUND

Atrial fibrillation (AF) is the commonest cardiac arrhythmia, characterised by an irregularly irregular pulse, and an absence of P waves on electrocardiogram (ECG). It is a major independent risk factor for thromboembolic disease, particularly stroke with which it is associated with a fivefold increase in risk.

Prevalence data for AF have been notoriously difficult to ascertain with estimates of 5–10% in the population aged ≥65 years. A review of four large community-based studies of AF suggested that the overall community prevalence in the US is 0.89%. Our primary care studies in the UK indicate that over 10% of people aged >75 years experience AF[1] and 4% of people with AF are undiagnosed.[2] Prevalence increases sharply with age: 2.3% of people aged ≥40 years; 5.9% of people aged ≥65 years, and 10% of those >80 years. The vast majority (84%) of people with AF are ≥65 years.

AF is a particularly important risk factor for stroke in older people: while 15% of all strokes are associated with the arrhythmia, it is associated with 36% of strokes in people aged >80 years. The incidence of new cases of AF in people aged ≥65 years is of the order of 1% per annum.

The risk of stroke can be reduced through the use of anticoagulant agents; for example, warfarin has been found to be consistently effective for the prevention of ischaemic stroke with a reduction in the incidence of all strokes of 68% (95% confidence interval = 50% to 79%), representing an absolute annual reduction of 3.1% (P<0.001). Newer agents (dabigatran, rivaroxaban, and apixaban) have been found in large randomised controlled trials (RCTs) to be at least as effective and are now to be considered alongside warfarin when deciding on anticoagulation.[3]

Despite the robust evidence base for effective stroke prevention through use of anticoagulation, there remain many people who have undetected AF. Those that are known receive either no or ineffective treatment, particularly aspirin, and there remain concerns over the quality of anticoagulant control for those patients receiving warfarin. Therefore, the key points for general practice are:

- take a pulse — to increase case finding;
- risk assess all patients for stroke and, if necessary, bleeding risk;
- prescribe effective anticoagulation for stroke prevention and modify anticoagulation bleeding risk where possible; and
- ensure effective therapeutic control for patients receiving warfarin therapy.

RECOMMENDATIONS FROM PRIMARY CARE RESEARCH

Screening for atrial fibrillation

Our SAFE trial was designed to identify the most cost-effective method for detecting AF.[1] Screening for AF in older people fulfils many of the Wilson-Jungner criteria for a screening programme. It is a common and important condition which can be diagnosed by means of a simple test (ECG), and the risk of serious sequelae such as stroke can be dramatically reduced by treatment.

Approximately 5% of total NHS expenditure can be attributed to stroke, and there would be expected to be about 1000 new cases of stroke per annum in a typical health authority with a half-million population. Therefore, any programme that might lead to an important reduction in stroke incidence needs serious consideration, because of the potential for health gain and the potential for reduced overall NHS expenditure. Screening for AF might be one such programme since, in population terms, AF is an important risk factor for stroke (associated with 15% of all strokes) and anticoagulation provides a highly-effective treatment to reduce this

risk. A meta-analysis of RCTs has shown a 68% relative risk reduction in patients' with AF receiving oral anticoagulation.[4] It has been estimated that optimal treatment of AF in the population could reduce the overall incidence of stroke by 10%. However, before implementing screening programmes, unresolved questions about how screening should be conducted needed answers.

The SAFE study answered several questions on both the epidemiology of AF and the optimal screening strategy. This large scale multicentred RCT utilised 50 UK primary care practices (25 intervention and 25 control), with intervention practice patients randomly allocated to systematic or opportunistic screening for 12 months. Opportunistic screening comprised pulse taking and ECG if the pulse was irregular. The principle outcome measure was screened AF detection rates compared to the detection rate in routine care. The study included 4936 control, 4933 opportunistic screening, and 4933 systematic screening patients. In control practices the baseline prevalence of AF was 7.9% compared to 6.9% in intervention practices. Routine practice (control) identified 47 new cases of AF (incidence 1.04% per year): 243 opportunistic patients had irregular pulse, 177 had ECG, yielding 31 new cases (0.69% per year), and 44 cases were detected outside screening (total 1.64% per year). A total of 2357 systematic patients had ECG yielding 52 new cases (1.1% per year): 31 would have been detected by targeted screening, a further 21 by total population screening, and 22 further cases were detected outside screening (total 1.62% per year). The principal conclusion from the SAFE study was that active screening will identify an additional one-third of cases of AF. Opportunistic screening identified as many of these cases as systematic screening for considerably less effort, and should be promoted in primary care as long as a high level of coverage can be maintained. Although the UK has not established a formal screening programme on these data, the cost effectiveness of opportunistic pulse checks in those aged ≥65 years is now advocated in National Institute for Health and Care Excellence (NICE) and European Society of Cardiology AF guidelines on the basis of the SAFE trial.

Secondary analysis of the SAFE data has demonstrated that those patients detected through screening have at least as high risk of stroke as those detected through routine care.[5] Furthermore, recently published data on the reliability of AF detection technologies compare well with opportunistic pulse checking.[6]

Assessment of stroke and bleeding risk

The most recent NICE AF guideline recommends using the CHA_2DS_2-VASc (previously $CHADS_2$) score to assess stroke risk, mainly to identify those at low risk of stroke who require no treatment, and the HAS-BLED score to assess bleeding risk, mainly to identify the modifiable risk factors (uncontrolled hypertension, labile INR results, interacting drugs, and excess alcohol consumption). It is important to note that the HAS-BLED score should not be used to decide whether to recommend use of anticoagulation to patients.

Treatment of stroke risk in patients with AF

All patients with a CHA_2DS_2-VASc of ≥2 should be offered anticoagulation, while those with a CHA_2DS_2-VASc of 1 should be considered for anticoagulation. Those patients with a CHA_2DS_2-VASc of 0 should receive no therapy. It is specifically stated that aspirin therapy should not be offered solely for stroke prevention in AF. For patients receiving a vitamin K antagonist it is also recommended to calculate the individual time in therapeutic range (TTR, using the Rosendaal equation) at each visit, for the previous 6 months and excluding the first 6 weeks of treatment.

Primary care-led anticoagulation. Our early research demonstrated the efficacy and safety of primary care management of patients receiving oral anticoagulation (predominantly warfarin). The first two-centre study demonstrated that patients could be managed in primary care through utilisation of computerised decision support software,[7] while the second, larger study established the Birmingham Model for oral anticoagulation management with the addition of near patient testing for INR measurement and practice training.[8] This work helped validate, quantify, and establish the feasibility of primary care-led anticoagulation and subsequently underpinned the shift of anticoagulant services from secondary to primary care in the UK and led to the inclusion of anticoagulation as an national enhanced service within the 2004 General Medical Services (GMS) contract. This primary care model has also been adopted internationally.

Changed guidance on the role of aspirin in AF stroke prevention. While there was evidence for the effectiveness of oral anticoagulation

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in stroke prevention, this evidence was less robust for patients aged ≥75 years. There was concern that the bleeding risks with warfarin balanced out the benefits of treatment leading to physician uncertainty of whether aspirin was a safer option in this population, although they were perversely at greater risk of stroke, supported by a meta-analysis of post hoc analyses of those aged ≥75 years from the warfarin versus aspirin trials. This uncertainty, based on observational data, was directly answered in our BAFTA trial which showed warfarin as 65% more effective than aspirin, but of equal safety in terms of bleeding risk, in the high risk older population (>75 years) population.[9]

These data have now been used to update the van Walraven meta-analysis, using individual patient data and the enriched older patient numbers, which confirmed the therapeutic benefit with comparable safety of warfarin in over 75s.[10] Indeed, this meta-analysis also confirmed the increasing bleeding risks and declining efficacy of aspirin with age, crossing the line of unity at around age 70 years, in contrast to warfarin. These data have been key in the revised guidance in international guidelines, including NICE, to avoid aspirin use in AF stroke and either offer anticoagulation only, or no treatment if stroke risk is low.

Importance of good therapeutic control of warfarin. Given the inevitable bleeding risks with warfarin, the revised European and NICE AF guidelines stress the importance of good warfarin control, recommending that TTR is above 65%. This target is achievable in primary care with appropriate training, using validated INR decision support software and point-of-care INR tests, as in the Birmingham Model in practices[8] or self-management by patients.[11]

Novel anticoagulation agents. Over the past 5 years, two major new classes of anticoagulants have been launched, the direct thrombin and factor Xa inhibitors. Both classes are rapid onset, short-acting agents, with few drug and no food interactions, and do not require monitoring (unlike the slow onset, very long duration, and multiple interactions of warfarin). The newer agents are at least as effective as warfarin and safer with regard to major bleeds. Although there are, as yet, no antidotes, in practice the short half-life of <12 hours has meant that major bleeds when they occur are no riskier than with warfarin. The main limitations of the newer agents are in patients with significant renal impairment, especially with dabigatran which is nearly 80% renally excreted. NICE has recommended that choice of anticoagulant, including the newer agents, should be discussed with and determined by patients.

FURTHER WORK

While SAFE and BAFTA have been important in terms of changing clinical practice and inclusion in major national and international guidelines, they have also been important in terms of generating further research. This has included primary care evaluations of near-patient INR test kits,[12] computerised decision support software,[13] evaluating stroke risk scores,[14] the important potential for patient self-management of oral anticoagulation,[11,15] further work on optimising case finding,[16] and investigation into the real-life treatment of AF.[17]

Taken in conjunction with historic data demonstrating overwhelmingly the superiority of anticoagulation compared to aspirin for stroke prevention in older people, our primary care research over the past two decades has made major and important contributions to continuing to change international guidance aimed at reducing stroke in patients with AF.

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Provenance

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